# Intervention Cut ED Visits for Blacks With Diabetes

BY DOUG BRUNK San Diego Bureau

SAN DIEGO — An intensive intervention conducted by a nurse case manager and community health worker over 18 months helped reduce visits to the emergency department, and possibly hospitalizations, among urban African Americans with type 2 diabetes, Tiffany Gary, Ph.D., reported at the annual scientific sessions of the American Diabetes Association.

"This intervention is designed to test a novel approach to improve diabetes care in urban African Americans," said Dr. Gary of Johns Hopkins University, Baltimore. "The final results from our 24- and 36-month studies will determine the significance.

She and her associates randomized 542 African Americans with type 2 diabetes to either an intensive intervention group or a minimal intervention group.

Participants in the minimal interven-

tion group received reminders every 6 months about preventive screenings in the form of mailings and phone calls from a lay health educator with a high school education.

Participants in the intensive intervention group received individualized care from a nurse case manager and a community health worker. The nurse case manager saw the patients in the clinic yearly, Dr. Garv said.

"She used algorithms and intervention

effects in the nursing infant have not been documented, withdrawal can occur in breast-feeding infants when maternal administration of an opioid analgesic is discontinued. Because of the potential for serious adverse reactions in nursing infants from the oxycodone present in Combunox, a decision should be made whether to discontinue nursing or to discon-tinue the drug, taking into account the importance of the drug to the mother. **Periatic Use** 

**cliatific Use** the placebo-controlled, clinical studies of pain following dental surgery, 109 patients between e ages of 14 and 17 years were administered a single doss of Combunox. No apparent differ-ces were noted in the safety of Combunox in patients below and above 17 years of age. mbunox has not been studied in patients under 14 years of age.

Combinitors has not Deen subjects in clinical studies of Combinors, 89 patients were 65 and over, while 37 patients were 75 and over. No overall differences in stately were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be nueled out. However, heceuse the elderly may be more sensitive to the renal and gastrointestinal effects of nonsteroidal anti-inflammatory agents as well as possible increased risk of respiratory depres-sion with opioids, extra caution should be used when treating the elderly with Combunox.

Sion With Options, extra clautors and a second seco

rse Events Which Occurred at a Frequency of ≥ 1% and at a Higher Incidence than in the Placebo Group in Single Dose Studies

	5/400 mg (n=923)	400 mg Ibuprofen (n=913)	5 mg Oxycodone HCI (n=286)	Placebo (n=315)
ligestive				
lausea	81 (8.8%)	44 (4.8%)	46 (16.1%)	21 (6.7%)
omiting	49 (5.3%)	16 (1.8%)	30 (10.5%)	10 (3.2%)
latulence	9 (1.0%)	7 (0.8%)	3 (1.0%)	0
lervous System				
omnolence	67 (7.3%)	38 (4.2%)	12 (4.2%)	7 (2.2%)
lizziness	47 (5.1%)	21 (2.3%)	17 (5.9%)	8 (2.5%)
kin and Annendages				

Appendages
15 (1.6%) 7 (0.8%) 4 (1.4%) Adverse events that were reported by at least 1% of patients taking Combunox but were at a greater incidence in the placebo treader gateries were fever, headence and provide the set of th 1 (0.3%)

stem: eughoria, insomna, nervousness. Respiratory System: hypoxia, lung disorder, aryngits. Urogenital System: urinary retention. Worse events that Occurred in the Multiple Dose study in at least 2% of patients treated with mburox include the following: Body as Whote: asthenia (33%), fewer (3.0%), headche 20%). Cardiovascular System: vasodilation (3.0%). Digestive System: constigation (4.5%), hrrithes (2.1%), dyspepsia (2.1%), nausea (25.4%), vomiting (4.5%). Nervous System: tizz-ss (12.2%), comolence (17.4%). Neusea (25.4%), vomiting (4.5%). Nervous System: tizz-ss (12.2%), comolence (17.4%). Neusea (25.4%), vomiting (4.5%). Nervous System: tizz-ss (12.2%), somolence (17.4%). Neurous System: tizz-ss (12.2%), somolence (17.4%). Neurous System: tizz-st (12.5%), Somolence (17.4%). The following. Body as Whote: back pain, ills, infection. Cardiovascular System: thrombophilebits. Hemic and Lymphatic System: chymosis. Metavolic and Nutritional Disorders: hypokalemia, Musculoskeletal System: hirlis. Nervous System: abnormal binking, anviety, hyperkinesia, hypertonia. Skin and pendages: rash. Special Senses: amblyopia, taste perversion. Urogenital System: urinary quency.

arthritis. Nervous System: abnormal thinking, anxiety, hyperkinesia, hyp

OVERDOSAGE

OVERDOSAGE Following an acute overdosage, toxicity may result from oxycodone and/or ibuprofen. Signs and Symptoms: Acute overdosage with oxycodone may be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and dammy skin, constricted pupils, bradycardia, or hypotension. In severe cases death may occur. The toxicity of lbuprofen overdose is dependent on the amount of drug ingested and the time legased since ingestion, atthough individual response may vary, necessitating individual evalu-ation of each case. Atthough uncommon, serious toxicity and death have been reported in the medical literature with lbuprofen overdosage. The most frequently reported symptoms of ibuprofen overdose linclude abdominal pain, nausea, vomiting, lethargy, and drowsiness. Other central nervous system symptoms include headache, linnitus, CMS depression, and seizures. Cardiovascular toxicity, including hypotension, bradycardia, tachycardia, and atrial fibrillation, have also been reported.

Particular and a start including improvension, brackparatine, europeande, en a anan normatour, have also been reported. Treatment of a patent airway and institution of assisted or controlled ventilation. Supportive measures (including oxygen and vasopressors) should be employed in the management of circulatory shock and pulmonary edema accompanying overdose, as indicated. Cardiac arrest or arrlyth-mass may require cardiac massages or defibrilitation. The narcotic antagonist naloxone hydrochlo-ride is a specific antidote against respiratory depression, which may result from overdosego or unusual sensitivity to narcotics including oxygoone may exceed that of the naloxone, the patient should be kept under continuous surveillance and repeated doses of the antagonis-tenda charade charcoal may help in reducing the absorption and reabsorption of thugoten-teres is not sefective if initiated during the absorption and reabsorption of thugoten-teres is not sefective if initiated during the absorption and reabsorption of thugoten-tion of gaties contents. A Schedue Charade area for the site of the antagonist A Schedue Cill Narcotic.

Forest Pharmaceuticals, Inc.

11/04 © 2004 Forest Laboratories Inc. action plans that were standardized and evidence based," she added.

The nurse case manager also provided written feedback to the primary care physicians, as well as verbal feedback, emails, and pages as necessary.

The community health workers were high school graduates who were native to the communities of Baltimore. "They saw the participants in their homes and in the community," Dr. Gary said. "They also implemented standarized algorithms and action plans. However, their focus was to hone in on the family environment and social support."

Current estimates suggest that the yearly cost of the program is about \$608 per patient, but data are still being analvzed.

The study was carried out in six primary care clinics affiliated with a managed

**Community health** workers saw study participants in the home and community. Their main task was to hone in on the family environment and social support.

care organization in Baltimore. It remains to be seen whether the intervention is cost effective and could be used in other settings and patient populations, Dr. Gary noted. Participants in both interventions at-

tended a baseline and follow-up interview, where the investigators obtained data on demographics, health care use and behaviors, and clinical characteristics. They also obtained data on diabetes-related emergency department visits and hospitalizations.

At baseline, participants had a mean age of 58 years and most (74%) were female. About one-third (35%) had annual household incomes of less than \$7,500 per year, and 33% were married.

More than half (57%) had hemoglobin A<sub>1c</sub> levels higher than 7%; 73% had blood pressure readings greater than 130/80 mm Hg, and 77% had HDL cholesterol levels that exceeded 40 mg/dL.

In addition, 39% reported at least one visit to the emergency department within the past year, and 23% reported having a diabetes-related hospitalization within the past year.

At 18 months, no significant differences were seen between the two intervention groups in terms of hemoglobin A<sub>1c</sub> levels, blood pressure, or lipids.

However, those who participated in the intensive intervention group had significantly fewer visits to the emergency department, compared with their counterparts in the minimal intervention group, which translated into a rate ratio of 0.78.

A trend toward fewer hospitalizations was also seen among those who participated in the intensive intervention group, compared with their counterparts in the minimal intervention group, but the rate ratio of 0.84 did not reach statistical significance.

Combunox≻ (Oxycodone HCl and Ibuprofen) Tablets 5 mg/400 mg

FOREST LABORATORIES CII Rx only Brief Summary: For complete details, please see full prescribing information for Combunox. INDICATIONS AND USAGE Combunox tables are indicated for the short term (no more than 7 days) management of acute, moderate to severe pain.

moderate to severe pain. CONTRAINDICATIONS Combunox should not be administered to patients who have previously exhibited hypersensitiv-ity to oxycodone HC, louporter, or any of Combunox's components, or in any situation where opioids are contraindicated. This Includes patients with significant respiratory depression (in ummonitored settings or the absence of resuscitative equipment) and patients with acute or severe bronchia samma or hyperactable. Combunox is contraindicated in any patient who have or severe bronchia samma or hyperactable. Combunox is contraindicated in any patient who have or severe bronchia samma or hyperactable. Combunox is contraindicated in any patient who have or severe bronchia NMICas. Anaphylic Bieus. Componence and the same and the same patients (see WARNINGS - Anaphylicatolia Reactions, and PFECAUTIONS. Prevesting Asthma). Patients is nown to be hypersensitive to other opioids may exhibit cross-sensitivity to oxycodone. WARNINGS

e and Diversion of Opioids contains oxycodone, which is an opioid agonist, and a Schedule II controlled sound is a sought by abusers and the potential for being abused and are sought by abusers and the potential for being abusers and are sought by abusers and the potential for being abusers and are sought by abusers and the potential for being abusers and are sought by abusers and the potential for being abusers and are sought by abusers and the potential for being abusers and are sought by abusers are sought by Combunox contains oxycodone, which is an opioid agonist, and a Schedule II controlled substance. Opioid agonists have the potential for heigh abused and are sought by abusers and people with addiction disorders, and are subject to diversion. Combunox can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing Combunox in situations where the physi-cian or pharmacist is concerned about an increased risk of misuse, abuse or diversion (see PNUs ABUSE-NND DEFENDENCE).

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optensive Effect history, tile all opioid analgesiss, may cause severe hypotension in an individual whose abi-to maintan blood pressure has been compromised by a depiletel blood volume, or after con-rent administration with drugs such as phenothazines or other agents which compromise omotor tone. Combunox may produce orthostatic hypotension in ambuilatory patients, nhunox, like all opioid analgesiss, should be administered with caution to patients in circu-ry shock, since vasodilatation produced by the drug may further reduce cardia cupture and the second seco

blood pressure. Head injury and Increased Intracranial Pressure The respiratory depressant effects of opioids and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, opioids produce adverse reactions that may obscure the clinical course of patients with head injuries. Acute Abdominal Conditions The administration of opioids may obscure the diagnosis or clinical course of patients with acute adverse in the clinical course of patients with nead injuries.

abdominal conditions. Gastrointestinal (GI) Effects Serious gastrointestinal toxicity, such as inflammation, bleeding, ulceration, and perfor the stomach, small intestime or large intestine, can occur at any time, with or without symptoms, in patients treated with non-steroidal anti-inflammatory drugs (NSADB) ibuproflen. Minor upper GI problems, such as dyspepsia, are common and may also occu time druing NSADD therapy. Therefore, physicians and patients should remain alert for ul and bleeding even in the absence of previous GI tract symptoms. Even short term therap without civit.

and bleeding even in the absence of previous GI tract symptoms. Even short term therapy is not without risk. NSAIDs should be prescribed with extreme caution in those with a prior history of ulcer disease or gastrointestinal bleeding. Most spontaneous reports of fataI GI events are in elderly or debil-itated patients and, therefore, special care should be taken in treating this population. To min-mize the potential risk for an adverse GI event the treatment period should be of the shortest possible duration. For high risk patients, alternate therapies that do not involve NSAIDs should be considered. In addition to a past history of ulcer disease, pharmacoepidemiological studies have identified several other o-charapies or co-morbid conditions that may increase the risk for GI bleeding such as treatment with oral corticosteroids, treatment with anticoagulants, longer duration of NSAID therapy, moking, and alcoholism. Anaphylactoid Reactions Anaphylactoid reactions may occur in patients without known prior exposure to Combunox.

Anaphylactoli Reactions are correct in patients without known prior exposure to Combunox. Combunox should not be given to patients with the asprint fraid or a history of angioedema. The triad byically occurs in asthmatic patients who experience rhinitis with or vithout nasa lodyns, or who exhibit severe, potentially fatal bronchospasm after taking asprint or other NSADS, Fatal reactions to NSADE have been reported in such materies (see CONTRAINDICATIONS and PRECAUTIONS - Pre-existing Asthma). Emergency help should be sought when anaptrijactoid reactions provide the second secon

Cition occurs. vanced Renal Disease patients with advanced kidney disease, treatment with Combunox is not recommended, wever, if Combunox therapy must be initiated, due to the NSAID component, close monitor-of the patient's kidney function is advisable (see PRECAUTIONS - Renal Effects).

In on the parameter stating, interesting the products, Combunox should be avoided in late pregnancy seven of the NSAID-containing products, Combunox should be avoided in late pregnancy occurs with Alcohol and Drugs of Abuse Oxycodone may be expected to have additive effects when used in conjunction with alcohol, other opioids, or illicit drugs that cause central nervous system depression.

## PRECAUTIONS General Special Risk Patients

Special Risk Patients As with any opioid analgesic agent, Combunox tablets should be used with caution in elderly or debilitated patients, and those with severe impairment of hepatic, pulmonary or renal function, hypothyroidism, Addions's disease auche alcoholism, convulsive disorbers, DNS depression or coma, delirium tremens, kyphoscoliosis associated with respiratory depression, toxic spo-chosis, prostatic, hypertophy or urethral stricture. The usual preactidinors should be observed and the possibility of respiratory depression, postural hypotension, and altered mental states envolve the uset in mind

I the possibility of respiratory over-valid be kept in mind. Ein Pancreat/DBiliary Tract Disease mbunox may cause spasm of the sphincter of Oddi and should be used with caution in first with Diliary tract disease, including acute pancreatitis. Opioids like Combunox may se increases in the serum anylase level.

Cough Reflex Oxycodne suppresses the cough reflex: as with other opioid containing products, caution should be exercised when Combunox is used postoperatively and in patients with pulmonary disease. Effect on Diagnostic Signs The arthypretic and anti-inflammatory activity of ibuprofen may reduce fever and inflammation, thus diminishing their utility as diagnostic signs in detecting complications of presumed nonin-tections; monifirmatory patient is consistent signs.

fectious, noninflammatory painful conditions. Hepatic Effects As with other NSAIDs, biuprofen has been reported to cause borderline elevations of one or more liver enzymes: this may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. Notable (3 times the upper limit of normal) elevations of SBPT (L1) or SBOT (KSP) occurred in controlled clin-ical traits in less than 1% of patients. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver tests are coursed, should be evaluated to revience of the development of more severe hepatic reactions while on therapy with Combunos. Severe hepatic reactions, including auxilication causes of fatal hepatitis, have been reported with iburofen as with other NSAIDs. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or I systemic maintestations occur (e.g. existion) like, rask the reported with caution is abias to reorgener developilia, rask, etc., Combunox stonid be discontinued. Rerail Effects Caution is hould be used when initiating treatment with Combunox in patients with considerable deripdration. It is advisable to rehydrate patients first and then start therapy with Combunos. Advanced Renal Disease). As with other NSAIDs, long-term administration of bibprofen has resulted in renal papillary necrosis and other renal pathologic changes. Renal toxicity has also been seen in patients in which renal protestion.

As this necrois and other renal pathologic changes. Renal toxicity has also been seen in patients in which renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of a nonsteroidal anti-Inflammanory drug may cause a doss-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may

precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dystunction, those taking diuretics and ACE inhibitors, and the delery. Discontinutation of nonsteroid ant inhiminimatory drug therapy is usually fol-lowed by recovery to the pretreatment state. Ibuprofer metabolitis are eliminiated primarily by the kidneys. The extent to which the metabo-lites may accumulate in patients with renal failure has not been studied. Patients with signifi-cantly impaired renal function should be more closely monitored. Hematological Effects Ibuprofer intexe to early some studied. Patients with signifi-cantly impaired renal function should be more closely monitored. Hematological Effects Ibuprofer, like other NSAIDS, can inhibit platelet aggregation but the effect is quantitatively less and of shorter duration than that seen with aspirin. Ibuprofen has been shown to prolong bleedi-ing time in normal subjects. Because this prolonged bleeding effect may be exagerated in patients with under/king NSAIDS, including ibuprofen. This may be due to fluid retention, Gl loss, or an incompletely described effect upon erythropoiesis. Fluid Retention and Edema Have been reported in association with ibuprofen; therefore, the drug should be used with caution in patients with a history of cardiac decompensation, hypertension or heart failure. Pre-existing Asthma Patients with asthma may heve aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive patients, Combunox should not be administered to patients with its form of aspirin sensitivity patients, combunox should be the administered to patients with his form of aspirin sensitive patients, combunox should be administered to patients with his form of aspirin sensitive patients with acuudin in patients with caution in patients with caution in aptients with caution aspirin sensitive patients, benchunox should be used wintinations and patients with aspirin sensiti

sensitivity and should be used with caution in patients must be determined. Aseptic meningitis Aseptic meningitis with fever and coma has been observed on rare occasions in patients on Ibuprofer therapy. Although it is probably more likely to occur in patients with systemic lupus erythematous and related connective tissue diseases. It has been reported in patients who do not have an underlying chronic disease. It signs or symptoms of meningits develop in a patient on Combunov, the possibility of its being related to ibuprofen should be considered.

Into new an underlying informe bases in signs of symptoms or interinguis betted in a patient on Comburox, similar to other opioid-containing analgesics, may impair mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery, patients should be cautioned accordingly. The combination of this product with alcohol and other CNS depressants may produce an addi-tec NS depression and should be avoided. Comburox can be abused in a manner similar to other opioid agonists, legal or illicit. Paintes should task the durg only for a slong as it is prescribed, in the amounts prescribed, and no more frequently than prescribed. Comburox, like other drugs containing ibuprofen, is not free of side effects. The side effects of these drugs can cause discomfort and, rarely, there are more serious side effects, such as gas should be unstructed to report any signs or symptoms of gastrointestinal bleeding, blurred vision or other eye problems, skin rash, weight gain, or edema. Laboratory Tests

Use of a misuace of report and signs or a sign or edem. hore reye problems, skin rash, weight gain, or edem. horatory Tests lecrease in hemoglobin may occur during Combunox therapy, and elevations of liver enzymes y be seen in a small percentage of patients during Combunox therapy (see PRECAUTIONS -matological Effects and PRECAUTIONS - Hepatic Effects), patients with severe hepatic or renal disease, effects of therapy should be monitored with liver i/or renal function tests.

And/or renal function tests. **Drug Interactions** Oxycodone Oxycodone is metabolized in part to oxymorphone via the cytochrome P<sub>ess</sub> isoenzyme CYP2D6. While this pathway may be blocked by a variety of drugs (e.g., certain cardiovascular drugs and antidepressants), such blockade has not yet been shown to be of clinical significance with this agent. However, clinicians should be avaired of this possible interaction. Anticholinergies: The concurrent use of anticholinergies with oxycodone preparations may pro-to another interaction.

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## Pregnancy Teratogenic Effects

Pregnancy Category C Animal studies to assess the potential effects of the combination of oxycodone and ibuprofen on embry-felal development were conducted in the rat and rabbit model. Pregnant rats were treated by oral gavage with combination doess of oxycodone:buprofen mg/kg/day (0252, 00,540, 1.080, 07, 20,160) on days 7-16 of gestation. There was no evi-dence for developmental toxicity or teratogenicity at any does, although maternal toxicity was noted at doess of 0.540 and above. The highest does tested in the rat 2.00160 mg/dg/day) on a body sur-face area (mg/ms) basis. This does was associated with maternal toxicity (death, clinical signs, decreased BW).

face area (mg/m²) basis. This dose was associated with maternal toxicity (death, clinical signs, decreased BW). Pregnant rabbits were treated by oral gavage with combination doses of oxycodone/buprofen (0.83:0, 0.75:6, 15:012:0:30:024 mg/kg/day) orgestation days 7:19. Oxycodone/buprofen treatment was not teratogenic under the conditions of the assay. Maternal toxicity was noted at doses of 1.5:120 (reduced body weight and food consumption) and 3:240 mg/kg/day (mortality). The no adverse effect level (MOAEL) for maternal toxicity, 0.75:60 mg/kg/day, is avained at the proposed maximum daily human dose based upon the body surface area. Developmental toxicity, as evidenced by delayed ossification and reduced fetal body weight and foot his <u>approximately</u> 5 times the MHHD on a mg/m² basis, and is likely due to maternal toxicity. The fetal NOAEL of 1.50:120 mg/kg/day is <u>approximately</u> 1.5 times the MHHD on a mg/m² basis. There are no adequate and well-controlled studies in pregnant women. Combunox should be used during pregnancy only if the potential hereit usifies the potential risk to the fetus. Because of the bluprofen component, Combunox should not be used during the third trimsetter of pregnancy because it could cause problems in the unborn child (premature dosure of the ducus arthriosus and pulmonary hypertension in the fetus/menater). Labor and Delivery

Declaise of pregnancy because it could cause proments in the deutering of pregnancy because it could cause proments in the fetus/heonate). Labor and Delivery Combunox should not be used during the third trimester of pregnancy due to the potential for ibuprofen to inhibit porstaglandin synthetase which may prolong pregnancy and inhibit labor. Oxycodone is not recommended for use in women during and immediately prior to labor and delivery because oral opioids may cause respiratory depression in the newborn. **Nursing Mothers** Ibuprofen is not transferred to breast milk in significant quantities. The American Academy of Pediatrics classified lourofen as compatible with breastleeding. In studies using a 1 mcg/mL assay, louprofen was not detected in the milk of lactating profers. Oxycodone is excreted in neonates whose mothers were taking narcotic analgesics during pregnancy. Although adverse

agent. However, clinicians should be avare of this possible interaction. Anticholinergists: The concurrent use of anticholinergics with oxycodone preparations may pro-duce paralytic leus. CNS Depressants: Patients receiving narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hyponotics or other CNS depressants (including alcohol) concomi-tantly with oxycodone may exhibit an additive CNS depressants (including alcohol) concom-tantly with oxycodone may exhibit an additive CNS depressants (including alcohol) concom-tantly with oxycodone may exhibit an additive CNS depressants (including alcohol) concom-tantly with oxycodone may exhibit an additive CNS depressant any result if these drugs are taken in combination with the usual dosage of oxycodone. When such combined therapy is con-mplated; the dose of one or both agents should be administered with caution to patients who have received or are receiving a course of therapy with a pure opioid agonist analgesics use as oxycodone. In this situation, MCAOIs JMCOIs have been reported with caution to patients who have received or are receiving a course of therapy with a pure opioid agonist analgesics of a course of the oxycodone and/or may precipitale withdrawal symptoms in these patients. Monoamine Oxidase Inhibitors, the recombined to repatient the effects of at least one opioid drug causing anxiety, confusion and significant depression of respiration or oram. The use of oxycodone is not recommended for patients taking MAOIs or within 14 days of stopping such treatment. Neuromusular Blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.