Postoperative analgesia with epidural fentanyl

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A retrospective analysis of 133 patients who received continuous epidural fentanyl for postoperative analgesia is presented. Using a concentration of 5 μ g/mL of fentanyl, patients received continuous epidural infusions for 24 to 72 hours postoperatively. The average rate of infusion was 60 μ g/h. A total of 59.3% of the patients received no additional narcotics; 26.3% required supplemental narcotics during the first 24 hours only. Three percent had the infusion discontinued because it provided poor pain control. Side effects were less than, or comparable to, those of epidural morphine. Respiratory depression, defined as a respiratory rate of less than 8, or apnea did not occur. Urinary retention occurred in one patient. Pruritus occurred in 4% (6 patients). Nausea occurred in 25.5%, a rate comparable to that which occurred with epidural morphine. No side effects occurred in 70.6% of the patients reviewed. These data show that epidural fentanyl provides good to excellent pain relief with minimal side effects.

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The control of postoperative pain with epidural narcotics has been widely studied.¹⁻⁵ Improved ventilation, as compared with parenteral narcotics, has also been documented.^{5,6} Epidural morphine has been most often studied and seems almost ideal for postoperative analgesia. Its long duration of action and low incidence of side effects are its main advantages. However, respiratory depression or apnea, which can occur with epidural morphine, can be life-threatening and requires close monitoring of the patients.¹

Epidural fentanyl provides a similar quality of postoperative analgesia, yet it seems to have a decreased incidence of respiratory depression.^{3,7} It has a short term of effect (3 to 4 hours after each bolus dose). However, continuous infusions of fentanyl solutions epidurally have been used to provide safe, long-term (more than 24 hours) postoperative analgesia in general surgical patients.⁴ A continuous infusion allows more precise titration of doses while maintaining adequate blood levels of the drug. The purpose of this study was to provide a retrospective analysis of the use of continuous epidural fentanyl in 133 postsurgical patients in a community hospital setting.

Materials and methods

After receiving the approval of the hospital's bioethics committee, we reviewed the charts of 133 patients who had received continuous infusion of

Table 1
Types of Surgical Procedures Performed in
Patients Who Received Continuous Epidural
Infusion of Fentanyl for Postoperative
Pain Relief (N = 133)

Type of procedure	No. of patients	%*
• Abdominal, total	73	54.9
Upper	31	23.3
Lower	42	31.6
• Gynecologic	27	20.3
• Obstetric	11	8.3
• Orthopedic	8	6.0
• Thoracic	9	6.8
• Vascular	5	3.8

*Percentage total exceeds 100 because of rounding.

epidural fentanyl for postoperative analgesia between March 1987 and May 1988. The side effects associated with the epidural narcotics and any supplemental narcotics used were recorded for each patient and results were compiled. Patients were American Society of Anesthesiology (ASA) class II through IV. There were 91 women (68.4%) and 42 men (31.6%). A wide variety of surgical procedures were performed (Table 1). At surgery, a total of 117 patients received a general anesthetic while 16 patients received continuous epidural anesthesia. Ages ranged from 18 to 90 years (median, 57.4 years). This included 45 patients (33.8%) older than 70 years of age.

The method of postoperative analgesia had been discussed with all patients at the time of the preoperative visit, and informed consent had been obtained in all cases. The type of anesthetic given for the surgery was not a determining factor in the decision regarding postoperative analgesia.

Epidural catheters were placed during the anesthetic period, either before or after the surgical procedure. The epidural catheter was inserted at the L2-3 or L3-4 interspace and threaded approximately 3 to 5 cm cephalad into the epidural space. All patients received an injection of a test dose of 2 mL of 1.5% lidocaine. A microfilter was placed at the end of the epidural catheter, and all additional medications were injected through the filter. Before transportation of the patient to the recovery room, 100 µg of fentanyl was injected into the epidural catheter. On the patient's arrival in the recovery room, the continuous infusion of epidural fentanyl solution was started. An infusion pump was used to control the rate of infusion. The con-

centration of the drip was 5 µg/mL of fentanyl, using 500 µg of fentanyl in 90 mL of preservative-free 0.9% saline solution. The infusion was started at a rate of 8 to 13 mL/h (average, 60 µg/h) and titrated to control pain. Continuous monitoring of vital signs and side effects was carried out by the nursing staff, beginning in the recovery room. Respiration and pulse rates were recorded hourly, as were the incidences of nausea and vomiting, pruritus, and complaints of urinary retention. Any supplemental narcotics given to the patient were also recorded.

All patients remained under the service of the department of anesthesia while the drips were being infused. No sedatives or narcotics were administered without the department's approval. Most patients were monitored on the general surgical ward, but some patients were transferred to the intensive care unit and were monitored there, as dictated by the type of surgery they had undergone.

Results

The majority of the patients (74%) had continuous epidural analgesia for 72 hours. The epidural doses of patients who had undergone cesarean section were discontinued after 18 to 24 hours. At this point, most obstetric patients were requesting showers, and their pain was well-controlled by oral pain medications.

No additional pain medications were administered to 79 patients (59.4%). Only 35 patients (26.3%) required supplemental pain medications during the first 24 hours. Epidural analgesia was discontinued in four patients due to inadequate pain control. All four of these patients continued to complain of inadequate pain relief despite parenteral administration of narcotics.

No side effects occurred in 70.6% of the patients. No patient had apnea. Floor nurses monitored ventilatory status by measuring respiratory rates. There were no documented respiratory rates of less than 10 per minute, the rate at which administration of naloxone would be required.

Thirty-four patients (25.6%) experienced nausea. In nine of these patients, the complaint was transient and occurred only once during the first 24 hours after surgery. All nine patients had received a general anesthetic.

Six patients reported having pruritus. Three

of these patients had undergone cesarean sections. After receiving 0.4 mg of naloxone administered intravenously, they had no further itching. A 29-year-old woman had her epidural infusion discontinued 24 hours after a cholecystectomy when severe itching was unrelieved by diphenhydramine and naloxone. The itching dissipated after the epidural infusion was discontinued.

One patient, a 50-year-old woman, had urinary retention as well as symptoms of nausea, vomiting, and pruritus. The symptoms developed more than 24 hours after cholecystectomy. At the patient's request, we continued the epidural fentanyl infusion for a total of 24 hours because she was receiving excellent pain relief (Table 2).

Discussion

Fentanyl is a highly lipid-soluble narcotic. Its onset of action in the epidural space is more rapid than that of morphine. Fentanyl's lipid solubility accounts for its rapid uptake by the opiate receptors in the spinal cord; this uptake leaves only minimal amounts to be absorbed systemically.^{1,7} This rapid uptake also prevents the formation of residual cerebrospinal fluid concentrations of the drug that can migrate rostrad and cause delayed respiratory depression, an occurrence seen with epidural morphine.^{1,8} Onset of action of epidural fentanyl, 0.1 mg, is 4 to 10 minutes, with complete relief attained in 20 minutes. The duration of action is 5 to 6 hours.¹ Continuous infusions of smaller doses allow long-term relief with more precise titration of drug dosages.

It is well documented that epidural narcotics can provide superior pain relief when compared with parenteral narcotics.^{1,2} Epidural morphine has been reported to provide excellent to complete postoperative analgesia in 37% to 46% of patients.^{9,10} In our study, no additional narcotics were required in 59.3% of the patients.

Side effects observed with epidural narcotics include nausea, vomiting, pruritus, urinary retention, and respiratory depression.⁸ Studies have shown that the incidence of these side effects when narcotics are used is similar, no matter what the method of administration.¹¹

Table 2
Complications in Patients Receiving Continuous Epidural Infusion of Fentanyl for Postoperative Pain Relief (N = 133)

Complication	No. of patients* (n = 39)	%
Nausea	34	25.5
Pruritus	6	4.5
Urinary retention	1	0.7
Respiratory depression	0	0

*One patient had urinary retention in addition to nausea and pruritus.

Our own data for epidural fentanyl indicated similar to fewer instances of side effects than those described for epidural morphine. In addition, our chart review showed no infections or hematomas from the use of the epidural catheter.

Because of its short serum half-life and lipid solubility, epidural fentanyl causes fewer instances of respiratory depression. The improvement in ventilatory status also seen with this drug may outweigh the risks of respiratory depression.^{3,7,12} In 1987, Negre and associates⁷ showed a decrease in the ventilatory response to CO₂ with epidural fentanyl. Renaud and colleagues³ showed a decreased minute ventilation and an increased end tidal CO₂, but minute volume and end tidal CO₂ were mild and nonsignificant when doses of epidural fentanyl of 1 µg/kg/h were used. We believe that epidural fentanyl may be safer than epidural morphine when considering respiratory depression. Our own experience with epidural morphine has shown several instances of respiratory depression requiring administration of naloxone, including one episode of apnea. Despite the improved safety and effectiveness, we continue to closely monitor patients to whom we have administered postoperative epidural narcotics.

Nausea and vomiting are frequent postoperative occurrences. A 30% incidence of nausea and vomiting has been reported when intravenous or intramuscular opioids are used postsurgically.^{1,6} The reported incidence of nausea after epidural morphine ranged from 16%

to 50%.^{1,9,13} In our study, the incidence of nausea with epidural fentanyl was 25%.

Six (4.5%) of the patients complained of pruritus during epidural fentanyl administration. In five of the patients, the itching was transient. An incidence of up to 90% has been reported with epidural morphine.^{14,15} No relationship between the dose of epidural narcotics and the incidence of pruritus has been determined.¹⁴ Severe pruritus appears to affect about 1% of patients. This incidence compares with that in our study: one patient had her epidural dose discontinued because of severe itching.

Because of the high incidence (up to 100%) of urinary retention with epidural morphine,¹⁵⁻¹⁷ it had been the protocol at our institution for patients receiving epidural narcotics to have a Foley catheter inserted during surgery and maintained in place until the administration of epidural narcotics was discontinued. The low incidence (0.7%) of urinary retention with epidural fentanyl has changed that practice. Foley catheters are inserted preoperatively only when needed to monitor urinary output or when the type of surgical procedure being performed indicates the need. The catheters are removed at the discretion of the surgeon (usually within 24 hours).

Our use of epidural fentanyl in elderly patients revealed no increased incidence of side effects when compared with epidural morphine. In patients of extreme age (older than 85 years), decreased doses of narcotics were used with excellent analgesia and minimal, if any, side effects.

Conclusion

The use of continuous epidural fentanyl provides postoperative pain relief with minimal side effects. The nursing staff and patients have expressed greater satisfaction with epidural fentanyl as compared with epidural morphine. Despite the low incidence of side effects, it is still important to monitor patients after

receiving continuous infusion of epidural fentanyl. We believe administration of epidural fentanyl by continuous infusion can be done safely on a general surgical floor.

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[†]P<0.05 vs placebo.

*The most common side effects that were significant versus placebo were dizziness, somnolence, and fatigue. Syncope has been reported, but rarely (<1%).

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CARDURA® (doxazosin mesylate) Tablets Brief Summary of Prescribing Information INDICATIONS AND USAGE

CARDURA (doxazosin mesylate) is indicated for the treatment of hypertension. CARDURA may be used alone or in combination with diuretics or beta-adrenergic blocking agents. There is limited experience with CARDURA in combination with angiotensin converting enzyme inhibitors or calcium channel blockers.

CONTRAINDICATIONS

CARDURA is contraindicated in patients with a known sensitivity to quinazolines (e.g., prazosin, terazosin).

WARNINGS

Syncope and "First-dose" Effect:

Doxazosin, like other alpha-adrenergic blocking agents, can cause marked hypotension, especially in the upright position, with syncope and other postural symptoms such as dizziness. Marked orthostatic effects are most common with the first dose but can also occur when there is a dosage increase, or if therapy is interrupted for more than a few days. To decrease the likelihood of excessive hypotension and syncope, it is essential that treatment be initiated with the 1 mg dose. The 2, 4, and 8 mg tablets are not for initial therapy. Dosage should then be adjusted slowly (see DOSAGE AND ADMINISTRATION section) with increases in dose every two weeks. Additional antihypertensive agents should be added with caution.

Patients being titrated with doxazosin should be cautioned to avoid situations where injury could result should syncope occur.

In an early investigational study of the safety and tolerance of increasing daily doses of doxazosin in normotensives beginning at 1 mg/day, only 2 of 6 subjects could tolerate more than 2 mg/day without experiencing symptomatic postural hypotension. In another study of 24 healthy normotensive male subjects receiving initial doses of 2 mg/day of doxazosin, seven (29%) of the subjects experienced symptomatic postural hypotension between 0.5 and 6 hours after the first dose necessitating termination of the study. In this study 2 of the normotensive subjects experienced syncope. Subsequent trials in hypertensive patients always began doxazosin dosing at 1 mg/day resulting in a 4% incidence of postural side effects at 1 mg/day with no cases of syncope.

In multiple dose clinical trials involving over 1500 patients with dose titration every one to two weeks, syncope was reported in 0.7% of patients. None of these events occurred at the starting dose of 1 mg and 1.2% (8/664) occurred at 16 mg/day.

If syncope occurs, the patient should be placed in a recumbent position and treated supportively as necessary.

PRECAUTIONS

General:

1. Orthostatic Hypotension:

While syncope is the most severe orthostatic effect of CARDURA, other symptoms of lowered blood pressure, such as dizziness, lightheadedness, or vertigo, can occur, especially at initiation of therapy or at the time of dose increases. These were common in clinical trials, occurring in up to 23% of all patients treated and causing discontinuation of therapy in about 2%.

In placebo controlled titration trials orthostatic effects were minimized by beginning therapy at 1 mg per day and titrating every two weeks to 2, 4, or 8 mg per day. There was an increased frequency of orthostatic effects in patients given 8 mg or more, 10%, compared to 5% at 1-4 mg and 3% in the placebo group.

Patients in occupations in which orthostatic hypotension could be dangerous should be treated with particular caution.

If hypotension occurs, the patient should be placed in the supine position and, if this measure is inadequate, volume expansion with intravenous fluids or vasopressor therapy may be used. A transient hypotensive response is not a contraindication to further doses of CARDURA.

2. Impaired liver function:

CARDURA should be administered with caution to patients with evidence of impaired hepatic function or to patients receiving drugs known to influence hepatic metabolism (see CLINICAL PHARMACOLOGY). There is no controlled clinical experience with CARDURA in patients with these conditions.

3. Leukopenia/Neutropenia:

Analysis of hematologic data from patients receiving CARDURA in controlled clinical trials showed that the mean WBC (N=474) and mean neutrophil counts (N=419) were decreased by 2.4% and 1.0% respectively, compared to placebo, a phenomenon seen with other alpha blocking drugs. A search through a data base of 2400 patients revealed 4 in which drug-related neutropenia could not be ruled out. Two had a single low value on the last day of treatment. Two had stable, non-progressive neutrophil counts in the 1000/mm³ range over periods of 20 and 40 weeks. In cases where follow-up was available the WBCs and neutrophil counts returned to normal after discontinuation of CARDURA. No patients became symptomatic as a result of the low WBC or neutrophil counts.

Information for Patients:

Patients should be made aware of the possibility of syncope and orthostatic symptoms, especially at the initiation of therapy, and urged to avoid driving or hazardous tasks for 24 hours after the first dose, after a dosage increase, and after interruption of therapy when treatment is resumed. They should be cautioned to avoid situations where injury could result should syncope occur during initiation of doxazosin therapy. They should also be advised of the need to sit or lie down when symptoms of lowered blood pressure occur, although these symptoms are not always orthostatic, and to be careful when rising from a sitting or lying position. If

1 Begin all patients with CARDURA 1 mg once daily to minimize side effects. Evaluate supine and standing blood pressure. Prescribe CARDURA 2 mg once daily, if necessary.

2 Evaluate for blood pressure control. Prescribe 4 mg once daily, if necessary.

3 Evaluate for blood pressure control. Prescribe 8 mg once daily, if necessary. Maximum recommended dosage is 16 mg once daily.

dizziness, lightheadedness, or palpitations are bothersome they should be reported to the physician, so that dose adjustment can be considered. Patients should also be told that drowsiness or somnolence can occur with doxazosin, requiring caution in people who must drive or operate heavy machinery.

Drug Interactions:

Most (88%) of plasma doxazosin is protein bound. *In vitro* data in human plasma indicate that CARDURA has no effect on protein binding of digoxin, warfarin, phenytoin or indomethacin. There is no information on the effect of other highly plasma protein bound drugs on doxazosin binding. CARDURA has been administered without any evidence of an adverse drug interaction to patients receiving thiazide diuretics, beta blocking agents, and nonsteroidal anti-inflammatory drugs.

Drug/Laboratory test interactions:

None known.

Cardiac Toxicity in Animals:

An increased incidence of myocardial necrosis or fibrosis was displayed by Sprague-Dawley rats after 6 months of dietary administration at concentrations calculated to provide 80 mg doxazosin/kg/day and after 12 months of dietary administration at concentrations calculated to provide 40 mg doxazosin/kg/day (150 times the maximum recommended human dose assuming a patient weight of 60 kg). There is no evidence that similar lesions occur in humans.

Carcinogenesis, Mutagenesis and Impairment of Fertility:

Chronic dietary administration (up to 24 months) of doxazosin mesylate at maximally tolerated concentrations (highest dose 40 mg/kg; about 150 times the maximum recommended human dose of 16 mg/60 kg) revealed no evidence of carcinogenicity in rats. There was also no evidence of carcinogenicity in a similarly conducted study (up to 18 months of dietary administration) in mice. The mouse study, however, was compromised by the failure to use a maximally tolerated dose of doxazosin.

Mutagenicity studies revealed no drug- or metabolite-related effects at either chromosomal or subchromosomal levels.

Studies in rats showed reduced fertility in males treated with doxazosin at oral doses of 20 (but not 5 or 10) mg/kg/day, about 75 times the maximum recommended human dose. This effect was reversible within two weeks of drug withdrawal.

Pregnancy

Teratogenic Effects. Pregnancy Category B. Studies in rabbits and rats at daily oral doses of up to 40 and 20 mg/kg, respectively (150 and 75 times the maximum recommended daily dose of 16 mg, assuming a patient weight of 60 kg), have revealed no evidence of harm to the fetus. The rabbit study, however, was compromised by the failure to use a maximally tolerated dose of doxazosin. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, CARDURA should be used during pregnancy only if clearly needed.

Radioactivity was found to cross the placenta following oral administration of labelled doxazosin to pregnant rats.

Nonteratogenic Effects. In perinatal studies in rats, postnatal development at maternal doses of 40 or 50 mg/kg/day of doxazosin was delayed as evidenced by slower body weight gain and a slightly later appearance of anatomical features and reflexes.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when CARDURA is administered to a nursing mother.

Pediatric Use

Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

CARDURA has been administered to approximately 4000 patients, of whom 1679 were included in the clinical development program. In that program, minor adverse effects were frequent, but led to discontinuation of treatment in only 7% of patients. In placebo-controlled studies adverse effects occurred in 49% and 40% of patients in the doxazosin and placebo groups, respectively, and led to discontinuation in 2% of patients in each group. The major reasons for discontinuation were postural effects (2%), edema, malaise/fatigue, and some heart rate disturbance, each about 0.7%.

In controlled clinical trials directly comparing CARDURA to placebo there was no significant difference in the incidence of side effects, except for dizziness (including postural), weight gain, somnolence and fatigue/malaise. Postural effects and edema appeared to be dose related.

The prevalence rates presented below are based on combined data from placebo-controlled studies involving once daily administration of doxazosin at doses ranging from 1-16 mg. Table 1 summarizes those adverse experiences (possibly/probably related) reported for patients in these studies where the prevalence rate in the doxazosin group was at least 0.5% or where the reaction is of particular interest.

TABLE 1: ADVERSE REACTIONS DURING PLACEBO CONTROLLED STUDIES

	DOXAZOSIN (N=339)	PLACEBO (N=336)
CARDIOVASCULAR		
Dizziness	19%	9%
Vertigo	2%	1%
Postural Hypotension	0.3%	0%
Edema	4%	3%
Palpitation	2%	3%
Arrhythmia	1%	0%
Hypotension	1%	0%
Tachycardia	0.3%	1%
Peripheral Ischemia	0.3%	0%
SKIN APPENDAGES		
Rash	1%	1%
Pruritus	1%	1%
MUSCULOSKELETAL		
Arthralgia/Arthritis	1%	0%
Muscle Weakness	1%	0%
Myalgia	1%	0%
CENTRAL & PERIPHERAL N.S.		
Headache	14%	16%
Paresthesia	1%	1%

	DOXAZOSIN (N=339)	PLACEBO (N=336)
	Kinetic Disorders	1% 0%
	Ataxia	1% 0%
	Hypertonia	1% 0%
	Muscle Cramps	1% 0%
AUTONOMIC	Mouth Dry	2% 2%
	Flushing	1% 0%
SPECIAL SENSES	Vision Abnormal	2% 1%
	Conjunctivitis/Eye Pain	1% 1%
	Tinnitus	1% 0.3%
PSYCHIATRIC	Somnolence	5% 1%
	Nervousness	2% 2%
	Depression	1% 1%
	Insomnia	1% 1%
	Sexual Dysfunction	2% 1%
GASTROINTESTINAL	Nausea	3% 4%
	Diarrhea	2% 3%
	Constipation	1% 1%
	Dyspepsia	1% 1%
	Flatulence	1% 1%
	Abdominal Pain	0% 2%
	Vomiting	0% 1%
RESPIRATORY	Rhinitis	3% 1%
	Dyspnea	1% 1%
	Epistaxis	1% 0%
URINARY	Polyuria	2% 0%
	Urinary Incontinence	1% 0%
	Micturition Frequency	0% 2%
GENERAL	Fatigue/Malaise	12% 6%
	Chest Pain	2% 2%
	Asthenia	1% 1%
	Face Edema	1% 0%
	Pain	2% 2%

Additional adverse reactions have been reported, but these are, in general, not distinguishable from symptoms that might have occurred in the absence of exposure to doxazosin. The following adverse reactions occurred with a frequency between 0.5% and 1%: syncope, hyposthesia, increased sweating, agitation, increased weight. The following additional adverse reactions were reported by <0.5% of 3960 patients who received doxazosin in controlled or open, short- or long-term clinical studies, including interventional studies. *Cardiovascular System:* angina pectoris, myocardial infarction, cerebrovascular accident; *Autonomic Nervous System:* pallor; *Metabolic:* thirst, gout, hypokalemia; *Hematopoietic:* lymphadenopathy, purpura; *Reproductive System:* breast pain; *Skin Disorders:* alopecia, dry skin, eczema; *Central Nervous System:* paresis, tremor, twitching, confusion, migraine, impaired concentration; *Psychiatric:* paranoia, amnesia, emotional lability, abnormal thinking, depersonalization; *Special Senses:* parosmia, taste perversion, photophobia, abnormal lacrimation; *Gastrointestinal System:* increased appetite, anorexia, focal incontinence, gastroenteritis; *Respiratory System:* bronchospasm, sinusitis, coughing, pharyngitis; *Urinary System:* renal calculus; *General Body System:* hot flashes, back pain, infection, fever/rigors, decreased weight, influenza-like symptoms.

CARDURA has not been associated with any clinically significant changes in routine biochemical tests. No clinically relevant adverse effects were noted on serum potassium, serum glucose, uric acid, blood urea nitrogen, creatinine or function tests. CARDURA has been associated with decreases in white blood cell counts (See Precautions).

OVERDOSAGE

The oral LD₅₀ of doxazosin is greater than 1000 mg/kg in mice and rats. The likely manifestation of overdosage would be hypotension, for which the usual treatment would be intravenous infusion of fluid. As doxazosin is highly protein bound, dialysis would not be indicated.

DOSAGE AND ADMINISTRATION

DOSAGE MUST BE INDIVIDUALIZED. The initial dosage of CARDURA in hypertensive patients is 1 mg given once daily. Depending on the individual patient's standing blood pressure response (based on measurements taken at 2 hours postdose and 24 hours postdose), dosage may then be increased to 2 mg thereafter if necessary to 4 mg, 8 mg and 16 mg to achieve the desired reduced blood pressure. Increases in dose beyond 4 mg increase the likelihood of excessive postural effects including syncope, postural dizziness/vertigo, postural hypotension. At a titrated dose of 16 mg once daily the frequency of postural effects is about compared to 3% for placebo.

HOW SUPPLIED

CARDURA (doxazosin mesylate) is available as colored tablets for oral administration. Each tablet contains doxazosin mesylate equivalent to 1 mg (white), 2 mg (yellow), 4 mg (orange) or 8 mg (green) of the active constituent, doxazosin.

CARDURA TABLETS are available as 1 mg (white), 2 mg (yellow), 4 mg (orange) and 8 mg (green) scored tablets. Bottles of 100: 1 mg (NDC 0049-2750-66), 2 mg (NDC 0049-2760-66), 4 mg (NDC 0049-2770-66), 8 mg (NDC 0049-2780-66). Recommended Storage: Store below 86°F (30°C).

CAUTION: Federal law prohibits dispensing without prescription.

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