Alphapress®

Prazosin Hydrochloride USP

Description
Alphapress® 1: Each Tablet contains Prazosin 1mg.
Alphapress® 2: Each Tablet contains Prazosin 2mg.
Alphapress® XR 2.5: Each Extended Release Tablet contains Prazosin 2.5mg.
Alphapress® XR 5: Each Extended Release Tablet contains Prazosin 5mg.

INDICATIONS
Hypertension
Alphapress® XR/Alphapress® is indicated in the treatment of all grades of essential (primary) hypertension and of all grades of secondary hypertension of variec etiology. It can be used as the initial and sole agent or it may be employed in a treatment program in combination with a diuretic and/or other antihypertensive drugs as needed for proper patient response. Renal blood flow and glomerular filtration rate are not impaired by long-term oral administration and thus **Alphapress® XR/Alphapress®** can be used with safety in hypertensive patients with impaired renal function.

Left Ventricular Failure: Alphapress® XR/Alphapress® is indicated in the treatment of left ventricular failure. **Alphapress® XR/Alphapress®** may be added to the therapeutic regimen in those patients who have not shown a satisfactory response or who have become refractory to conventional therapy with diuretics, with or without cardiac glycosides.

Raynaud's Phenomenon And Raynaud's Disease: Alphapress® XR/Alphapress® indicated in the treatment of Raynaud's phenomenon and Raynaud's disease.

Benign Prostatic Hyperplasia: Alphapress® XR/Alphapress® is indicated as an adjunct in the symptomatic treatment of urinary obstruction caused by benign prostatic hyperplasia. It is also of value in patients awaiting prostatic surgery.

CONTRAINDICATIONS
Alphapress® XR/Alphapress® is contracindicated in patients with a known sensitivity to quinazolines.

WARNINGS
Pregnancy or Lactation
Although no teratogenic effects were seen in animal testing; the safety of **Alphapress® XR/Alphapress®** use during. pregnancy has not yet been established. The use of prazosin and a beta-blocker for the control of sever hypertension of 44 pregnant women revealed no drug-related fetal adnormalities or adverse effects. Therapy with prazosin was continued for as long as 14 weeks. **Alphapress® XR/Alphapress®** has also been used alone or in combination with other hypotensive agents in severe hypertension or pregnancy. No fetal or neonatal abnormalities have been reported with the use of **Alphapress® XR/Alphapress®**. There are no adequate and well controlled studies which establish the safety of **Alphapress® XR/Alphapress®** in pregnant women. **Alphapress® XR/Alphapress®** should be used during pregnancy only if in the opinion of the physician the potential benefit justifies the potential risk to the mother and fetus. **Alphapress® XR/Alphapress®** has been shown to be excreted in small amounts in human milk. Caution shold be exercised when **Alphapress® XR/Alphapress®** is adminsitered to nursing mothers.

Children: Alphapress® XR/Alphapress® is not recommended for the treatmet of children under the age of 12 years since safe conditions for its use have not been established.

Left Ventricular Failure: Alphapress® XR/Alphapress® is not recommended in the treatment of left ventricular failure due to mechanical obstrcution such as aortic valve stenosis, mitral valve stenosis, pulmonary embolism and restrictive pericardial disease. Adequate data are not yet available to establish efficacy in patients with left ventricular failure due to a recent myocardial infarction.

PRECAUTIONS
Hypertension: A very small percentage of patients have responded in an abrupt and exaggerated manner to the initial dose of **Alphapress® XR/Alphapress®**. Postural hypotension evidenced by dizziness and weakness, or rarely loss of consciousness, has been reported, particularly with the commencement of therapy, but this effect is readily avoided by initiating treatment with a low dose of **Alphapress® XR** and with small increases in dosage during the first one to two weeks of therapy. The effect when observed is not related to the severity of hypertension, is self-limiting and in most patients does not recur after the initial period of therapy or during subsequent dose titration steps. When instituting therapy with any effective antihypertensive agent, the patient should be advised how to avoid symptoms resulting from postural hypotension and what measures to take should they develop. The patient should be cautioned to avoid situations where injury could result should dizzines or weakness occur during the initiation of **Alphapress® XR/Alphapress®** therapy.

Left Ventricular Failure: When prazosin is initialy adminstered to patients with left ventricular failure who have undergone vigorours diuretic or other vasodilator treatment, particularly in higher than the recommended starting dose, the resultant decrease in left ventricular filling pressure may be associated with a significant fall in cardiac output and systemic blood pressure. In such patients, observance of the recommended starting dose of prazosin followed by gradual titration is particularly important. (See dosage and admininstration). Occasional patients with left ventricular failure the clinical efficacy of **Alphapress® XR/Alphapress®** has been reported to diminish after several months of tratment. In these patients there is usually evidence of weight gain or peripheral edema indicating fluid retention. Since spontaneous deterioration may occur in such severely ill patients a causal relationship to prazosin therapy has not been established. Thus, as with all patients with left ventricular failure, careful adjustment of diuretic dosage according to the patient's clinical condition is required to prevent excessive fluid retention and consequent relief of symptoms. In those patients without evidence of fluid retention, when clinical improvement has diminished; an ircrease in the dosage, of **Alphapress® XR/Alphapress®** will usually restore clinical efficacy.

Raynaud's Phenomenon and Raynaud's Disease: Because **Alphapress® XR/Alphapress®** decreases peripherea vascular resistance, careful monitoring of blood pressure during initial adminstration and titration of **Alphapress® XR/Alphapress®** is suggested. Close observation is especially recommended for patients already taking medication that are known the lower blood presssure.
Benign Prostatic Hyperplasia: Alphapress® XR/Alphapress® decreases peripheral vasular resistance and since many patients with this disorder are elderly, careful monitoring of blood preassure during initial administration and during adjustment of the dose of **Alphapress® XR/Alphapress®** is suggested. Close obervation is especially recommended for patients taking medications that are known to lower blood pressure.

DRUG INTERACTIONS
Alphapress® XR has been administered without any adverse drug interaction in clinical experience to date with the following : (1) cardiae-glycosides-digitails and digoxin; (2) hypoglycemic agents-insulin, chlorpropamide, phenformin, tolazamide, and tolbutamide; (3) tranquilizers and sedatives-chlordiazepoxide, diazepam and phenobarbital; (5) antiarrhytmic agents-procanamide, propranolol and quinidine; and (6) analgesic, antipyretic and anti-inflammatory agents-propxyphene, aspirin, indomethacin and phenylbutazone type.

ADVERSE REACTIONS
The most common reactions associated with **Alphapress® XR/Alphapress®** therapy are dizziness, headache, drowsiness, lack of energy, weakness, palpitations and nausea. In most instances side effects have disappeared with continued therapy or have been tolerated with no decrese in dosage of the drug. In addition, the following reactions have been associated with **Alphapress® XR/Alphapress®** therapy; vomiting diarrhea, constipation, abdominal discomfort and/or pain, liver function abnormalities, pancreatitis, edema, orthostatic hypotension, dyspnea, faintness, tachycardia, nervousness, vertigo, hallucinations, depression, parestnesia, rash, pruritus alopecia, lichen planus, urinary frequency, impotence, incontinece, priapism, blurred vision, reddened solera, epistaxis, tinnitus, dry mouth, nasal congestion, diaphoresis, fever, positve ANA liter, and arthralgia. Some of these reactions have occurred rarely, and in many instances the exact causal relationships have not been eastblished. Literature reports exist associating **Alphapress® XR/Alphapress®**, therapy with a worsening of pre-existing narcolepsy. A causal relationship is uncertain in these casses. The following have been observed in parients being managed for left ventricular failure with **Alphapress® XR/Alphapress®** when used in conjuction with cardiac glycosides and diuretics; drowsiness, dizziness, postural hypotension, blurred vision, edema, dry mouth, palpitations, nausea, diarrhea, impotences, headache, and nasal congestion. In most instances these occurrences have been mild to moderate in severity and have resolved with continued therapy or have been tolerated with no decrease in drug dosage. The most commonly although infrequently reported side effect in the treatment of Raynaud's Phenomenon/Disease was mild dizziness.

OVERDOSAGE
Accidental ingestion of at least 50 mg of **Alphapress® XR/Alphapress®** in a two year child resulted in profound drowsiness and depressed reflexes, No decrease in blood pressure was noted. Recovery was uneventful. Should overdosage lead to hypotension, support of the cardiovascular system is of first importance. Restoration of blood pressure and normalization of heart rate may be accomplished by keeping the patient in the supine position. If this measure is inadequate, shock should first be treated with volume expanders. If necessary, vasopressors should then be used. Renal function should be monitored and supported as needed. Laboratory data indicate **Alphapress® XR/Alphapress®** is not dialyzable because it is protein bound.

DOSAGE AND ADMINISTRATRATION
Alphapress® Tablet:
There is evidence that toleration is best when therapy is initiated with a low starting dose. During the first week, the dosage of **Alphapress®** should be adjusted according to the patient's individual toleration. Thereafter the daily dosage is to be ajdusted on the basis of the patient's response. Response is usually seen within one to 14 days if it is to occur at any particular dose. When a response is seen, therapy should be continued at that dosage until the degree of response has reaehed optimurn before the next dose increment is added.

Hypertension : For maximum benefit, small increases should be continued until the desired effect is achieved or a total daily dosage of 20 mg is reached. A diuretic or adrenergic beta blocking agent may be added to enhance efficacy. The maintenance dosage of **Alphapress®** may be given as a twice or three times daily regimen.

A. Patients Receiving No Antihypertensive Therapy. It is recommended that therapy be initiated with 0.5 mg given in the evening at bedtime then 0.5 mg b.i.d. or t.i.d for three to seven days. Unless poor toleration suggests the patients is unusually sensitive, this dosage should be increased to 1 mg given b.i.d. or t.i.d. for a further three to seven days. Thereafter, as determined by the patient's response to the blood pressure lowering effect, the dosage should be increased gradually to a total daily dosage of 20 mg given in divided doses.

B. Patients Receiving Diuretic Therapy With inadequate Control of Blood Pressure. The diuretic should be reduced to a maintenance dosage level for the particular agent and **Alphapress®** initiated with 0.5 mg h.s then proceeding to 0.5 mg b.i.d or t.i.d. After the initial period of observation, the dosage of **Alphapress®** should be gradually increased as determined by the patient's response.

C. Patients Receiving Other Antihypertensives But With Inadequate Control. Because some additive effect is anticipated, the other agent dosage level (e.g. beta-adrenergic blocking agents, methyldopa. reserpine, «Isnidine etc.) should be reduced and **Alphapress®** initiated at 0.5 mg h.s. then proceeding to 0.5 mg b.i.d, or t.i.d. Subsequent dosage increase, should be made depending upon the patient's response. There is evidence that adding **Alphapress®** to beta-adrenergic blocking agent, calicium antagonists or ACE inhibitors may bring about a substantial reduction in blood pressure. Thus, to low initial dosage regimen is strongly, recommended.

D. Patients With Moderate to Severe Gredes of Renal Impairment Evidence to date shows that **Alphapress®** dees not further compromise renal function when used in patients with renal impairment. Because some patients in this category have responded to small doses of **Alphapress®**, it is recommended that therapy be initiated at 0.5 mg daily and that dosage increases be instituted cautiously.

Left Ventricular Failure: The recommended starting dose is 0.5 mg two, three or four times a day, Dosage should be titrated according to the patent's clinical response, based on careful monitoring of cardiopulmonary signs and symptoms, and when indicated, hemodynamic studies. Dosage titration steps may be performed as often as every two or three days in patients under close medical supervision. In severely ill, decompensated patients, rapid dosage titiration over one to two days may be indicated and is best done when hemodynamic- monitoring is available In dininai studies, the therapeutic dosages ranged from 4 mg to 20mg daily in divided doses. Adjustment of dosage may be-required in the course of **Alphapress®** therapy in some patients to maintain optimal clinical improvement.

Suggested Starting Dosage: 0.5 mg b.i.d., t.i.d. or q.i.d. increasing to 4 mg in divided doses.

Usal Daily Maintenance Dosage: 4 mg once daily to 20 mg in divided doses.

Raynaud's Phenomenon And Raynaud's Disease: The recommended starting dosage is 0.5 mg b.i.d. given for a period of three to seven days. Dosage should be adjusted according to the patient's clinical response.

Suggested Starting Dosage: 0.5mg b.i.d.

Usual Daily Maintenance Dosage: 1mg or 2 mg b.i.d Doses up to 2 mg t.i.d. may be required for some patients.

Benign Prostatic Hyperplasia: The recommended starting dose is 0.5 mg twice daily given for a period of 3 to 7 days and should then be adjusted according to patient's clinical respones. The usual maintenance dose is 2 mg twice daily. The safety and efficacy of a total daily dosage greater than 4 mg has not been established. Therefore, total daily dosages greater than 4mg should be used with caution.

Alphapress® XR Tablet:
Alphapress® XR Extended Release Tablets must be swallowed whole and should not be bitten or divided. Therapy for hypertension with **Alphapress® XR** must be initiated at 2.5 mg once daily. The 5 mg dosage form of **Alphapress® XR** is not for initial dosing. Dosage may be increased slowly, in general over a 7 to 14 day period, depending on the response to each dose level. Doses above 20 mg once daily have not been studied.

Maintenance Dose: Dosage may be increased as clinically indicated to 20 mg given in once-daily doses.

Hypertensive patients controlled on **Alphapress®** Tablets alone or in combination with other antihypertensive medications may be switched to **Alphapress® XR** Extended Release Tablets at the equivalent or nearest higher total daily dose, e.g. **Alphapress®** Tablets 4 mg daily equivalent to **Alphapress® XR** Extended Release Tablets 5 mg once daily. Blood pressure measurements should be taken at the end of the dosing interval to assure adequate blood pressure control is maintained throughout the 24 hour period. Further titration may be necessary in some patients.

Addition of a diuretic or other antihypertensive agent to prazosin has been shown to cause an additive hypotensive effect.

STORAGE CONDITION:
Store in cool and dry place, away from direct light and children.

SUPPLY
Alphapress® 1: Each box contains 10x10 Tablets in blister packs.
Alphapress® 2: Each box contains 10x10 Tablets in blister packs.
Alphapress® XR 2.5: Each box contains 3x10 Extended Release Tablet in blister packs.
Alphapress® XR 5: Each box contains 3x10 Extended Release Tablet in blister packs.

Manufactured by
RENATA LIMITED
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