# Epliron®
(Eplerenone)

Highnoon

## COMPOSITION
**Epliron 25mg Tablet:** Each film-coated tablet contains:
Eplerenone 25mg
**Epliron 50mg Tablet:** Each film-coated tablet contains:
Eplerenone 50mg

## DESCRIPTION
Eplerenone is a selective aldosterone antagonist with properties similar to those of spironolactone.

## MECHANISM OF ACTION
Eplerenone binds to the mineralocorticoid receptor and blocks the binding of aldosterone, a component of the renin-angiotensin-aldosterone system (RAAS). Aldosterone binds to mineralocorticoid receptors in both epithelial (e.g., kidney) and nonepithelial (e.g., heart, blood vessels, and brain) tissues and increases blood pressure through induction of sodium reabsorption and possibly other mechanisms. Eplerenone has been shown to produce sustained increases in plasma renin and serum aldosterone, consistent with inhibition of the negative regulatory feedback of aldosterone on renin secretion. The resulting increased plasma renin activity and aldosterone circulating levels do not overcome the effects of eplerenone. Eplerenone selectively binds to human mineralocorticoid receptors relative to its binding to recombinant human glucocorticoid, progesterone, and androgen receptors.

## PHARMACOKINETICS
Peak plasma concentrations of eplerenone occur about 1.5 hours after an oral dose. They are dose proportional for doses of 25 to 100 mg and less than proportional above 100 mg. Protein binding primarily to $\alpha_1$ - acid glycoprotein is about 50%. Absorption is not affected by food. Eplerenone metabolism is mainly mediated by the cytochrome P450 isoenzyme CYP3A4. No active metabolites of eplerenone have been identified in human plasma. Less than 5% of a dose is excreted unchanged. About 32% of a dose is excreted in the feces and the remainder in the urine. The elimination half-life is approximately 4 to 6 hours. Eplerenone is not removed by dialysis.

## INDICATIONS
It is indicated in;
- Congestive Heart Failure Post-Myocardial Infarction
- Hypertension

## DOSAGE AND ADMINISTRATION
**Congestive Heart Failure Post-Myocardial Infarction**
It is given as adjunct to standard therapy for the management of heart failure in patients with clinical evidence of heart failure and LVEF ≤40% after a recent myocardial infarction. It is given in an initial dose of 25 mg daily, increasing to 50 mg daily within 4 weeks if tolerated. It should be withdrawn or the dose should be reduced to 25mg daily, or an alternate day, if hyperkalemia develops. It may be used in patients given mild to moderate CYP3A4 inhibitors, at a dose not exceeding 25mg daily.

**Hypertension**
In the management of hypertension, eplerenone may be given alone or with other antihypertensives. It is given in an initial dose of 50mg daily, increasing if necessary to a maximum of 50 mg twice daily. While eplerenone should not be given with potent CYP3A4 inhibitors, patients taking mild to moderate inhibitors may be given eplerenone; the initial dose should be reduced to 25mg daily. Higher dosages of eplerenone are not recommended because they have no greater effect on blood pressure than 100 mg and are associated with an increased risk of hyperkalemia.

## CONTRAINDICATIONS
**For all patients:**
- Serum potassium >5.5 mEq/L at initiation
- Creatinine clearance ≤30 mL/min
- Concomitant use with strong CYP3A4 inhibitors

For the treatment of hypertension:
- Type 2 diabetes with microalbuminuria
- Serum creatinine >2.0 mg/dL in males, >1.8 mg/dL in females
- Creatinine clearance <50 mL/min
- Concomitant use of potassium supplements or potassium- sparing diuretics.

## WARNINGS AND PRECAUTIONS
- Eplerenone should not be used in patients with hyperkalemia or severe renal impairment.
- It should be used with care in patients who are at increased risk of developing hyperkalemia; such patients include the elderly, those with diabetes mellitus, and those with some degree of renal or hepatic impairment.
- It should also be given with care to patients likely to develop acidosis.
- Serum electrolytes and blood urea nitrogen should be measured periodically.
- Check serum potassium and serum creatinine within 3-7 days of a patient initiating a moderate CYP3A4 inhibitors, ACE inhibitors, angiotensin-II blockers or non-steroidal-anti- inflammatories.
- Adjust the dose based on serum potassium level as shown in the Table:

| Serum Potassium (mEq/L) | Action | Dose Adjustment |
|---|---|---|
| < 5.0 | Increase | 25 mg every other day to 25 mg once daily<br>25 mg once daily to 50 mg once daily |
| 5.0–5.4 | Maintain | No adjustment |
| 5.5–5.9 | Decrease | 50 mg once daily to 25 mg once daily<br>25 mg once daily to 25 mg every other day<br>25 mg every other day to withhold |
| ≥6.0 | Withhold | Restart at 25 mg every other day when potassium levels fall to <5.5 mEq/L |

## ADVERSE REACTIONS
The following are the reported adverse event of the Eplerenone; hyperkalemia, increased creatinine, dizziness, cough, fatigue, flu-like symptoms, headache, angina pectoris/MI, increased GGT, Gynecomastia, abnormal vaginal bleeding, angioneurotic edema, rash, drowsiness, gastrointestinal disturbance including cramp and diarrhea, ataxia, mental confusion, hirsutism, deepening of voice, arrhythmia, asthenia, constipation, dyslipidemia, electrolyte imbalance, insomnia, muscle spasm, nausea, pain, skin reactions, syncope, vomiting, arterial thrombosis, cholecystitis, eosinophilia, flatulence, hyperhidrosis, hypothyroidism, increased risk of infection, malaise, numbness, postural hypotension and impotence.

## DRUG INTERACTIONS
- Eplerenone metabolism is predominantly mediated via CYP3A4. Do not use Eplerenone with drugs that are strong inhibitors of CYP3A4. These includes clarithromycin, telithromycin, itraconazole, ketoconazole, nefazodone, nelfinavir and ritonavir. Mild to moderate inhibitors of this enzyme such as erythromycin, fluconazole, saquinavir, and verapamil have a less marked effect, although a reduces dose of eplerenone may be necessary.
- Grape juice causes only a small increase in exposure to eplerenone.
- Inducers of this enzyme system such as carbamazepine, St John's Wort, Phenobarbital, Phenytoin and Rifampicin may reduce plasma concentration of eplerenone.
- The risk of hyperkalaemia increase when eplerenone is used in combination with an ACE inhibitor and/or an ARB.
- Lithium toxicity has been reported in patients receiving lithium concomitantly with diuretics and ACE inhibitors. Serum lithium levels should be monitored frequently if Eplerenone is administered concomitantly with lithium.
- The administration of other potassium-sparing antihypertensives with NSAIDs has been shown to reduce the antihypertensive effect in some patients and result in severe hyperkalemia in patients with impaired renal function. Therefore, when Eplerenone and NSAIDs are used concomitantly, monitor blood pressure and serum potassium levels.

## USE IN SPECIFIC POPULATIONS
**Pregnancy**
There are no adequate and well-controlled studies in pregnant women. Eplerenone should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nursing Mothers**
Many drugs are excreted in human milk and because of the unknown potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

**Pediatric Use**
Eplerenone has not been studied in hypertensive patients less than 4 years old because the study in older pediatric patients did not demonstrate effectiveness. Eplerenone has not been studied in pediatric patients with heart failure.

**Geriatric Use**
Patients greater than 75 years did not appear to benefit from the use of eplerenone. No differences in overall incidence of adverse events were observed between elderly and younger patients. However, due to age-related decreases in creatinine clearance, the incidence of laboratory-documented hyperkalemia was increased in patients 65 and older.

## OVERDOSAGE
No cases of human overdosage with eplerenone have been reported. The most likely manifestation of human overdosage would be anticipated to be hypotension or hyperkalemia. Eplerenone cannot be removed by hemodialysis. Eplerenone has been shown to bind extensively to charcoal. If symptomatic hypotension occur, supportive treatment should be instituted. If hyperkalemia develops, standard treatment should be initiated.

## DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from light.

## PRESENTATION
**Epliron 25mg Tablets:** Alu. Alu. Blister Pack of 2 x 7's.
**Epliron 50mg Tablets**: Alu. Alu. Blister Pack of 2 x 7's.

# ایپلیرون®
(ایپلیرینون)

## خوراک و ہدایات:
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔
خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

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