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# Azilsartan Medoxomil and Chlorthalidone Tablets (Edarbyclor)

??? ??????: 30 ??????/?????? 2017

**WARNINGS** The following potential adverse reactions with Edarbyclor, azilsartan medoxomil, or chlorthalidone and similar agents are included in more detail in the section of the label: **AND PRECAUTIONS**

- ] **WARNINGS AND PRECAUTIONS**Fetal toxicity [see
- ]**WARNINGS AND PRECAUTIONS** Hypotension in Volume-or Salt-Depleted Patients [see
- ]**WARNINGS AND PRECAUTIONS** Impaired Renal Function [see
- ]**WARNINGS AND PRECAUTIONS** Hypokalemia [see
- ]**WARNINGS AND PRECAUTIONS** Hyperuricemia [see

## Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Edarbyclor has been evaluated for safety in more than 3900 patients with hypertension; more than 700 patients were treated for at least 6 months and more than 280 for at least 1 year. Adverse reactions have generally been mild and transient in nature.

Common adverse reactions that occurred in the 8-week factorial design trial in at least 2% of Edarbyclor-treated patients and greater than azilsartan medoxomil or chlorthalidone are presented in Table 1.

**Table 1: Adverse Reactions Occurring at an Incidence of ? 2% of Edarbyclor-treated Patients and > Azilsartan medoxomil or Chlorthalidone**

| Edarbyclor 40 / 12.5, 40 / 25 mg (N=302) | Chlorthalidone 12.5, 25 mg (N=316) | Azilsartan medoxomil 20, 40, 80 mg (N=470) | Preferred Term |
|---|---|---|---|
| 8.9% | 1.9% | 1.7% | Dizziness |
| 2.0% | 1.3% | 0.6% | Fatigue |

Hypotension and syncope were reported in 1.7% and 0.3%, respectively, of patients treated with Edarbyclor.

Study discontinuation because of adverse reactions occurred in 8.3% of patients treated with the recommended doses of Edarbyclor compared with 3.2% of patients treated with azilsartan medoxomil and 3.2% of patients treated with chlorthalidone. The most common reasons for discontinuation of therapy with Edarbyclor were serum creatinine increased (3.6%) and dizziness (2.3%).

The adverse reaction profile obtained from 52 weeks of open-label combination therapy with azilsartan medoxomil plus chlorthalidone or Edarbyclor was similar to that observed during the double-blind, active controlled trials.

In 3 double-blind, active controlled, titration studies, in which Edarbyclor was titrated to higher doses in a step-wise manner, adverse reactions and discontinuations for adverse events were less frequent than in the fixed-dose factorial trial.

## Azilsartan Medoxomil

A total of 4814 patients were evaluated for safety when treated with azilsartan medoxomil at doses of 20, 40 or 80 mg in clinical trials. This includes 1704 patients treated for at least 6 months, of these, 588 were treated for at least 1 year. Generally, adverse reactions were mild, not dose related and similar regardless of age, gender and race.

Adverse reactions with a plausible relationship to treatment that have been reported with an incidence of ? 0.3% and greater than placebo in more than 3300

patients treated with azilsartan medoxomil in controlled trials are listed below:

diarrhea, nausea **Gastrointestinal Disorders:**

asthenia, fatigue **General Disorders and Administration Site Conditions:**

muscle spasm **Musculoskeletal and Connective Tissue Disorders:**

dizziness, dizziness postural **Nervous System Disorders:**

**Respiratory, Thoracic and Mediastinal Disorders: cough**

## Chlorthalidone

The following adverse reactions have been observed in clinical trials of chlorthalidone: rash, headache, dizziness, GI upset, and elevations of uric acid and cholesterol.

## Clinical Laboratory Findings with Edarbyclor

In the factorial design trial, clinically relevant changes in standard laboratory parameters were uncommon with administration of the recommended doses of Edarbyclor.

**Renal Parameters**

Increased blood creatinine is a known pharmacologic effect of renin-angiotensin aldosterone system (RAAS) blockers, such as ARBs and ACE inhibitors, and is related to the magnitude of blood pressure reduction. The incidence of consecutive increases of creatinine ? 50% from baseline and > ULN was 2.0% in patients treated with the recommended doses of Edarbyclor compared with 0.4% and 0.3% with azilsartan medoxomil and chlorthalidone, respectively. Elevations of creatinine were typically transient, or non-progressive and reversible, and associated with large blood pressure reductions.

Mean increases in blood urea nitrogen (BUN) were observed with Edarbyclor (5.3 mg/dL) compared with azilsartan medoxomil (1.5 mg/dL) and with chlorthalidone (2.5 mg/dL).

## Postmarketing Experience

The following adverse reactions have been identified during the postmarketing use of EDARBYCLOR. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Nausea
- Rash
- Pruritus
- Angioedema