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# Triamterene

Updated: June 18, 2015.

## OVERVIEW

### Introduction

Triamterene is a potassium-sparing diuretic widely used in the therapy of edema. Triamterene has been linked to rare cases of clinically apparent drug induced liver disease.

### Background

Triamterene (trye am' ter een) is an inhibitor of renal epithelial sodium channels in the late distal tubule and collecting ducts of the kidney. As a result, triamterene promotes a mild sodium diuresis, but maintains body potassium levels. Triamterene is used largely in therapy of edema and can be safely used in patients with cirrhosis. Because of its potassium-sparing actions, triamterene is also used in combination with thiazide or loop diuretics in an attempt to prevent hypokalemia. Triamterene was approved for use in the United States in 1964 and continues to be widely used with more than 20 million prescriptions filled yearly. Triamterene is available in tablets and capsules of 50 and 100 mg in generic forms and under the brand name of Dyrenium. The typical dose of triamterene is 50 to 200 mg daily in one or two divided doses. Triamterene is also available in fixed dose combinations with hydrochlorothiazide (Maxide, Dyazide and generically). The major side effects of triamterene are dizziness, fatigue, headache, dry mouth, hyperkalemia and dehydration.

### Hepatotoxicity

Triamterene therapy has been associated with rare instances of idiosyncratic, clinically apparent liver injury which have invariably been mild and anicteric. The liver injury typically arises after 4 to 12 weeks of therapy and the pattern of serum enzyme elevations is usually hepatocellular or mixed. Fever is a prominent symptom and the reaction is often more typical of drug-fever than hepatotoxicity (Case 1). Rash and eosinophilia can occur, but are usually not prominent. Autoantibodies are rare. All published cases of triamterene associated liver injury have been self-limited in course and resolved rapidly upon withdrawal.

Likelihood score: D (possible rare cause of clinically apparent liver injury).

### Mechanism of Injury

The mechanism of triamterene hepatic injury is unknown, but it likely to be due to hypersensitivity.

## Outcome and Management

Most instances of triamterene associated liver injury have been mild and rapidly reversible upon drug withdrawal. Rapid recurrence upon rechallenge has been reported. There is no evidence of cross reactivity to the hepatic injury with other diuretics.

References to the safety and potential hepatotoxicity of triamterene are provided in the overview on diuretics (updated October 2017).

Drug Class: Diuretics, Potassium-Sparing Diuretics

Other Drugs in the Subclass: Amiloride, Eplerenone, Spironolactone

# CASE REPORT

## Case 1. Triamterene induced fever and liver injury.

[Modified from: Nolan PJ, D'Arcy G. Triamterene drug fever and hepatitis. Med J Aust 1987; 147: 262. PubMed Citation]

A 44 year old woman developed fever, malaise and right upper quadrant pain one month after starting triamterene (100 mg daily) for peripheral edema. On examination, she was febrile (39$^{o}$ C) and had hepatic tenderness, but no rash or lymphadenopathy. Laboratory tests showed elevations in serum enzymes with AST 428 U/L and Alk P 170 U/L and slightly elevated total white blood cell count (12,000/μL). Abdominal ultrasound showed fatty liver, but no evidence of obstruction. Serum bilirubin levels, prothrombin time, hepatitis A or B markers and autoantibodies were not mentioned. Triamterene was stopped and her fever abated. She was discharged but presented 1 day later with recurrence of symptoms and fever. The white blood cell count was again raised and was accompanied by eosinophilia (2,520/μL). Serum enzymes were more elevated than before. Careful history revealed that she had restarted triamterene six hours before the reappearance of fever. Withholding further triamterene therapy was followed by resolution of fever and fall of white count, and liver test abnormalities to normal within 6 days.

### Key Points

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|---|---|
| Medication: | Triamterene (100 mg daily) |
| Pattern: | Hepatocellular (R=6.8) |
| Severity: | Mild (enzyme elevations without jaundice) |
| Latency: | 1 month initially, 1 day on rechallenge |
| Recovery: | 1-2 weeks |
| Other medications: | None |

### Comment

This patient developed drug fever one month after starting triamterene and had an accompanying increase in liver enzyme values. Rechallenge let to a prompt recurrence. These features are compatible with a hypersensitivity reaction with minor hepatic involvement. While rash and drug fever have been described with triamterene therapy, acute liver injury with jaundice has not.

# PRODUCT INFORMATION

**REPRESENTATIVE TRADE NAMES**

Triamterene – Generic, Dyrenium®

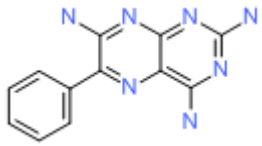
**DRUG CLASS**

Diuretics

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

# CHEMICAL FORMULA AND STRUCTURE

| DRUG | CAS REGISTRY NUMBER | MOLECULAR FORMULA | STRUCTURE |
|---|---|---|---|
| Triamterene | 396-01-0 | C12-H11-N7 |  |