MAYO CLINIC LABORATORIES

Test Definition: 17BFP

Fluticasone 17-B Carboxylic Acid, U

Overview

Useful For

Assessing compliance (recent exposure) to fluticasone propionate therapy

An aid in the evaluation of secondary adrenal insufficiency

Method Name

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Urine

Specimen Required

Collection Container/Tube: Clean, plastic urine collection container

Submission Container/Tube: Plastic, 10-mL urine tube (T068)

Specimen Volume: 5 mL

Collection Instructions:

1. Collect a random urine specimen.

2. No preservative.

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Minimum Volume

0.6 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	Frozen (preferred)	14 days	
	Refrigerated		
	Ambient		

Clinical & Interpretive

Clinical Information

Inhaled corticosteroids are the single most effective therapy for adult patients with asthma. Even low doses of inhaled corticosteroids have been shown to reduce mortality related to asthma. The September 2007 issue of Pediatrics reported that "Verification of (asthma) treatment adherence by objective measures remains necessary."(1) In this pediatric asthma adherence study, the 104 asthmatic children and their parents grossly overestimated their medication adherence. Over 1 of 3 responses reported full compliance to medications when no medications had been taken. Over 46% of individuals exaggerated their adherence by at least 25%. The authors concluded that "Under the best of conditions in this study, accuracy of self-report was insufficient to provide a stand-alone measure of adherence."(1,2)

Fluticasone propionate (FP) is an inhaled corticosteroid with anti-inflammatory and immunosuppressive properties commonly used for the treatment of asthma, airway inflammation, and allergic rhinitis. FP is typically well tolerated and has a low risk for adverse systemic effects when utilized at recommended therapeutic doses. However, noncompliance with recommended FP therapy may result in poorly controlled asthma or misinterpretation of the patient's therapeutic responsiveness. Patients with excessive exposure to FP may present with clinical features of Cushing syndrome, but with evidence of hypothalamus-pituitary-adrenal axis suppression, including suppressed cortisol levels. Conversely, a patient not administering the drug as recommended may have their therapeutic responsiveness interpreted, in error by the patient or clinician, as steroid-resistance.

FP has low oral bioavailability and high hepatic first-pass metabolism, which results in low plasma FP concentrations; any systemic levels are believed to occur through adsorption from the lungs. Native FP absorbed by the gastrointestinal tract (<1% total FP) is rapidly metabolized by cytochrome P450 isoform 3A4 to yield fluticasone 17-beta-carboxylic acid, its primary metabolic product.(3) Fluticasone 17-beta-carboxylic acid is pharmacologically inactive and has increased water solubility such that it is excreted in urine. Accordingly, fluticasone 17-beta-carboxylic acid is detected in urine in individuals recently exposed to inhaled FP therapy. Fluticasone 17-beta-carboxylic acid may be detected in urine as early as 16 to 24 hours following a patient's first administration of low dose (220 mcg) FP therapy. The window of detection for fluticasone 17-beta-carboxylic acid is 6 days following cessation of FP therapy.

Reference Values

Negative

Cutoff concentration: 10 pg/mL

Values for normal patients not taking fluticasone propionate should be less than the cutoff concentration (detection limit).

Interpretation

Elevated fluticasone 17-beta-carboxylic acid indicates recent exposure to fluticasone propionate (FP).

Fluticasone 17-beta carboxylic acid concentration <10 pg/mL indicates that the patient may not have administered inhaled FP therapy within the preceding 6 days. Validated concerns about suboptimal patient adherence to asthma controller medications should lead to patient and provider interactions to address potential compliance issues.

Cautions

Patients using fluticasone propionate (FP) therapy concurrently with a CYP3A4 inhibitor (eg, indinavir, nelfinavir, ritonavir, clarithromycin, itraconazole, ketoconazole, nefazodone, saquinavir, or telithromycin) may be at increased risk of adrenal insufficiency because of reduced FP metabolism to fluticasone 17-beta carboxylic acid, with increased levels of the corticosteroid FP and suppression of adrenal cortisol production.(4) In this situation, urine fluticasone 17-beta carboxylic acid concentrations may be below the limit of quantitation.

The Endocrine Laboratory should be notified if a urine specimen from a patient receiving fluorometholone therapy is to be analyzed for fluticasone 17-beta-carboxylic acid because fluorometholone is used as an internal standard in this method. If the laboratory is not notified and a significant amount of fluorometholone is present in the urine, a false-negative result may be reported.

Clinical Reference

1. Pearce RE, Leeder JS, Kearns GL: Biotransformation of fluticasone: in vitro characterization. Drug Metab Dispos 2006;34:1035-1040

2. Paton J, Jardine E, McNeill E, et al: Adrenal responses to low dose synthetic ACTH (Synacthen) in children receiving high dose inhaled fluticasone. Arch Dis Child 2006;91:808-813

3. Callejas SL, Biddlecombe RA, Jones AE, et al: Determination of the glucocorticoid fluticasone propionate in plasma by automated solid-phase extraction and liquid chromatography-tandem mass spectrometry. J Chromatogr B Biomed Sci Appl 1998;718:243-250

4. Bender BG, Bartlett SJ, Rand CS, et al: Impact of interview mode on accuracy of child and parent report of adherence with asthma-controller medication. Pediatrics. 2007;120:e471-477

5. National Asthma Education and Prevention Program: Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. J Allergy Clin Immunol. 2007 Nov;120(5 Suppl):S94-138

Performance

Method Description

Fluorometholone (4 ng/mL) internal standard is added to each calibrator, control, and urine sample. Fluticasone 17-beta-carboxylic acid is extracted from 1 mL of urine using an acid-based acetonitrile precipitation followed by methylene chloride liquid extraction of the supernatant. Following extraction, 60 mcL of the reconstituted sample extract is injected onto a high-performance liquid chromatography system and analyzed by tandem mass spectrometry. The mass spectrometer operates under the electrospray interface and is operated in the multiple-reaction monitoring positive mode. The calibration utilizes an 8-point calibration curve over a concentration range of 0 to 10,000 pg/mL.(Unpublished Mayo method)

PDF Report

No

Specimen Retention Time

2 weeks

Performing Laboratory Location

Rochester

Fees & Codes

Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

80299

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
17BFP	Fluticasone 17-B Carboxylic Acid, U	46952-8

Result ID	Reporting Name	LOINC®
89739	Fluticasone 17-B Carboxylic Acid, U	46952-8