NEW DRUG: Asenapine (Saphris®)

Asenapine (Saphris®) is a new atypical antipsychotic, second generation drug developed for the treatment of schizophrenia and acute mania associated with bipolar disorder. The drug is similar to other FDA approved atypical antipsychotic drugs currently in use such as Aripiprazole, Paloperidone, Ziprasidone, Clozapine, Quetiapine, Olanzapine, and Risperidone. Asenapine, initially approved in the United States in August 2009, is manufactured by Merck (formerly Schering-Plough) as 5- and 10-mg sublingual tablets that are to be taken twice a day.

General Information

IUPAC Name: (3aS,12bS)-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole

Chemical Formula: C₁₇H₁₆ClNO

Molecular Weight: 285.77 g/mol

Available: Sigma-Aldrich

Catalog A-7861: Asenapine Maleate,

C₁₇H₁₆ClNO·C₄H₄O₄, FW=401.84 g/mol

CAS Number: 65576-45-6

Pharmacology

Half-Life: ~ 24 hrs

Cmax ~ 4 ng/mL  ave T_max 1 hour, peak plasma 0.5 -1.5 hours, steady-state attained ~ 3 days

V_d ~20 - 25 L/kg

Bioavailability Sublingual: 35%, highly plasma proteins bound (95%)
If swallowed, low bioavailability (<2%) caused by extensive first-pass metabolism

Metabolism Glucuronidase- N+-glucuronide; others included N-desmethylasenapine, N-desmethylanapine N-carbamoyl glucuronide

Elimination 90% of the dose was recovered ~50% in urine and 40% in feces

Drug Interactions Paroxetine, Fluvoxamine

Toxicology

Extraction: Recovered by routine n-butyl chloride liquid:liquid basic drug extraction, including an acid back extraction.

Detection: GC/NPD: Limit of detection ~ 20 ng/ml  / GC/MS SIM: ~5.0 ng/ml

GC/MS: Ions 57, 215, 285 m/z

Elution order: Nortriptyline, Cyclobenzaprine, ASENAPINE, Sertraline, Citalopram

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NMS Labs: Analysis performed on Serum/Plasma and Urine, since April 2010. Detection by LC/MS/MS with a calibration range 0.10-15 ng/ml. 15 cases were analyzed, 0.71-5.6 ng/ml (n=9)

References

2. Personal Communication with Laura Labay, NMS Labs.