**REVIEW OF LITERATURE:**

**Faraat Ali\* et al1** : A sensitive, simple, fast, accurate and precise reverse phase high performance liquid chromatographic (RP-HPLC) method has been developed for the estimation of ziprasidone hydrochloride (ZH) in bulk and pharmaceutical dosage forms. The method was developed to analyze by using agilent zorbax C-8 (4.6mm X 150mm, 5 µm) column, mobile phase consisting of methanol and potassium dihydrogen orthophosphate buffer at pH 3.0, the flow rate of 1.5 ml/min and detection wavelength 229 nm and eluted at 22.2 min. The linearity ranges were 25% to 150 % for Ziprasidone hydrochloride. Analytical method was validated according to the International conference on Hormonization (ICH) guidelines for various parameters like specificity, linearity, precision, accuracy, LOD, LOQ and system suitability. Validated method was applied to the commercially available pharmaceutical dosage forms and obtained the desired result. So the method can be successfully applied for routine analysis.

**Keywords**: Ziprasidone, Validation, Acetonitrile, HPLC.

**KATARINA NIKOLIC et al 2:** Ziprasidone is the second generation antipsychotic drug with unique multipotent G-protein-coupled (GPCR) receptor binding profile. Since ziprasidone is a highly lipophilic and unstable compound, development of efficient method for a concurrent assay of ziprasidone and its main impurities was a very challenging task. The UHPLC-MS/MS method that we developed for simultaneous determination of ziprasidone and its main impurities (BITP, Chloroethyl-chloroindolinone, Zip-oxide, Zip-dimer, and Zip-BIT) was compared with some other related HPLC-UV methods of our own and other authorship. An increase of the mobile phase pH value from 2.5 to 4.7 units in the examined analytical methods influenced elution order of the investigated compounds. It was found out that the UHPLC-MS/MS method is more selective and sensitive than the earlier developed HPLC-UV method. Similar to our earlier HPLC-UV method, the UHPLC-MS/MS method is linear with a correlation coefficient (r) above 0.99 for all the analysed compounds, but with a negligibly lower precision and accuracy. Finally, with shorter analysis time, smaller column size and reduction of solvent consumption, UHPLC-MS/MS is assumed as a greener method than HPLC-UV for the ziprasidone purity assay. After transfer of the UHPLC-MS/MS method to the UHPLC-DAD system, suitability of the UHPLC-DAD method for routine control of ziprasidone and its main impurities is examined and confirmed based on the retained good selectivity, resolution and short analysis time.

**KEYWORDS:** ziprasidone, validation, ultra high performance liquid chromatography, tandem mass spectrometry, impurities

**Stephen E Nicolson and Charles B Nemeroff et al 3:** Ziprasidone is an atypical antipsychotic with a unique receptor-binding profile. Currently, ziprasidone is approved by the US Food and Drug Administration for the acute treatment of psychosis in schizophrenia and mania in bipolar disorder. When compared to certain other atypical antipsychotics, ziprasidone appears to have a relatively benign side effect profile, especially as regards metabolic effects eg, weight gain, serum lipid elevations and glucose dysregulation. Taken together, these data suggest that ziprasidone may be a first line treatment for patients with bipolar mania. However, ziprasidone is a relatively new medication for which adverse events after long-term use and/or in vulnerable patient populations must be studied. Unstudied areas of particular importance include the efficacy and safety of ziprasidone in the treatment of bipolar depression and relapse prevention of mania as, well as in the subpopulations of pregnant women, the elderly and pediatric patients. The emergence of mania in patients taking ziprasidone is another topic for further study.

**Keywords:**antipsychotic, bipolar disorder, mania, mood disorder, neuroleptic, ziprasidone

**William M. Greenberg, Leslie Clitrome et al 4:** Ziprasidone is a newer “atypical” or “second-generation” antipsychotic. Oral ziprasidone (ziprasidone hydrochloride) is approved by the U.S. Food and Drug Administration (FDA) for the treatment of schizophrenia, and acute manic or mixed episodes associated with bipolar disorder (with or without psychotic features). Ziprasidone intramuscular (ziprasidone mesylate) is FDA-approved for acute agitation in patients with schizophrenia. Oral ziprasidone appears efficacious, and has been shown to have some limited clinical advantages over chlorpromazine and haloperidol in ameliorating negative symptoms of schizophrenia. In Phase 2 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) for schizophrenia, ziprasidone did not match the clinical performance of olanzapine and risperidone, appearing closer in overall effectiveness to quetiapine. The rate of dose titration and the dose achieved may have an important bearing on ziprasidone's efficacy profile. In studies of usage for acute agitation in individuals with schizophrenia, intramuscular ziprasidone has been shown to be efficacious and relatively well tolerated. Regarding tolerability, ziprasidone, has important advantages in that it is not associated with clinically significant weight gain or adverse changes in cholesterol, triglycerides, or glycemic control, and patients may experience moderate improvement in these measures when switching to ziprasidone from a different antipsychotic agent. It also lacks significant persistent effects on prolactin levels, is not anticholinergic, and only infrequently causes extrapyramidal side effects or postural hypotension, although it can be associated with somnolence. This tolerability profile may be quite valuable in the treatment of some patients. Ziprasidone may prolong the electrocardiogram (ECG) QTc interval (QT interval corrected for heart rate by a standard algorithm), but after 5 years' clinical availability ziprasidone (by itself) does not appear to pose a substantial clinical problem in this regard. Therefore, ziprasidone may be considered a first-line drug option in the treatment of schizophrenia or manic episodes, but, in view of the differences among antipsychotic medications, drug selection should be guided by the patient's individual characteristics and situation.

**Marcio Versiani et al 5:** Ziprasidone is a second-generation antipsychotic currently marketed for the treatment of schizophrenia and bipolar mania. It has a unique receptor profile that includes high-affinity antagonist activity at 5-hydroxytryptamine (5-HT) 2A, D2, 1D and 2C receptors, a potent agonist activity at 5-HT1A receptors and a relatively high affinity for the 5-HT and noradrenaline transporters. The efficacy of ziprasidone in bipolar mania (current episode, manic or mixed) has been well demonstrated in three placebo-controlled trials. In a three-arm controlled study, ziprasidone was shown to be efficacious in dysphoric mania, whereas haloperidol was comparable to placebo. Open-label treatment for up to 52 weeks supported the sustained efficacy of ziprasidone in bipolar disorder. Combined with lithium, ziprasidone has been shown to be efficacious as an augmenting agent in the acute treatment of mania, with sustained efficacy up to 1 year. Ziprasidone was very well tolerated by patients with bipolar disorder and did not cause increased weight, glucose or lipid levels.

**Keywords::**Bipolar disorder, clinical trials , drug therapy, mania, ziprasidone.

**Emilio sacchetti , Alessandro galluzzo et al 6:** Ziprasidone, a benzisothiazolyl piperazine derivative of tiospirone, is a second-generation antipsychotic with high-affinity antagonism for 5-hydroxytryptophan (5HT)2A, 5HT2C, 5HT1D and D2 receptors, pre- and post-synaptic agonism for 5HT1A receptors, and inhibition of reuptake for serotonin and norepinephrine. Initially approved for the treatment of adults with schizophrenia, ziprasidone has more recently received supplementary indications for acute manic and mixed episodes and as maintenance therapy for people affected by bipolar disorder. Based on MEDLINE citations up to November 2010 and hand-searched references, this article relating to ziprasidone addresses its short- and long-term efficacy and safety, according to the results of randomized clinical trials, open-label studies and real-world experiences. Emerging evidence indicates that in patients with bipolar disorder, ziprasidone provides valid efficacy and remarkable safety when administered alone for the treatment of manic and mixed episodes. The same applies when ziprasidone is administered in combination with lithium or valproate for the prevention of affective relapses and recurrences. Any conclusion on the potential of ziprasidone as an antidepressant should be postponed because of insufficient evidence.

**Keywords::**Bipolar depression, bipolar disorder, mania, ziprasidone, manic-depressive disorder, mixed episode.

**Centorrino , Franca MD, Elizabeth ,Ross J et al6:** The antipsychotic drug ziprasidone, FDA-approved and introduced in the United States in February 2001 for the treatment of schizophrenia, appears to have similar efficacy but better tolerability than older antipsychotics and requires further evaluation under clinical conditions.