Atypical antipsychotics are increasingly used in bipolar disorder as antimanic, antidepressant, and maintenance treatments. Many of the clinical issues related to switching antipsychotics are similar between schizophrenia and bipolar disorder. These include similar motivations for switching due to limited efficacy and unacceptable adverse effects. Particular attention must be paid to the phase of treatment and coprescribed medications.

**ANTIPSYCHOTIC USE IN BIPOLAR DISORDER**

Although Elizabethan playwrights describe some psychiatric syndromes that are recognizable to the modern clinician, current psychiatric nosology has its roots in the late 19th century. The twin diagnoses that have preoccupied general psychiatrists for more than a century since then are schizophrenia and bipolar disorder. Originally formulated by Kraepelin as *dementia praecox* and *manic-depressive psychosis*, these were conceptualized as “functional” psychoses to distinguish them from clearly organic brain disorders such as the (then) recently described Alzheimer’s disease.

Kraepelin sought to disentangle these 2 scourges on the basis of careful clinical description and observation of natural history. Nevertheless, more than a century later, this diagnostic scheme is essentially still provisional. Recent research has reminded us of the shared etiopathogenesis of bipolar disorder and schizophrenia and has led to calls for an end to the “Kraepelinian dichotomy.” Although such calls may be premature, they do highlight how, on many levels, bipolar disorders and schizophrenia are inextricably linked.
therefore, to simple switching from one antipsychotic to another, but also includes augmentation.

**ADVERSE EFFECTS OF MEDICATION**

Medication should also be switched in bipolar disorder when patients suffer intolerable adverse effects that impair health or quality of life or result in nonadherence to medication. Adverse effects of antipsychotic medication used to treat bipolar disorder are similar to those reported for schizophrenia, and a general rule of thumb is to consider the side effects that are linked to the medication rather than the treated disorder. However, some, such as drug-induced motor side effects, may be even more pronounced in patients with bipolar disorder than in their counterparts with schizophrenia. A recent example of this was outlined in an article by Cavazzoni et al. These authors examined the rates of treatment-emergent extrapyramidal symptoms in patients with bipolar mania or schizophrenia during olanzapine clinical trials. Data from more than 4000 patients treated with olanzapine, haloperidol, or placebo were analyzed. Interestingly, patients with bipolar mania receiving haloperidol were more likely to develop extrapyramidal side effects than were patients with schizophrenia receiving haloperidol, although the atypical drug olanzapine caused similar amounts of treatment-emergent symptoms in both patient groups.

The weight gain and metabolic adverse effects of certain (but possibly not all) new antipsychotic medications have also been reported to occur when these drugs are used to treat bipolar disorder, and published data suggest a great similarity between the patient groups with respect to these metabolic consequences. This is particularly important as recent surveys have shown that adverse effects are a major driver of medication switch for bipolar disorder and may override efficacy considerations.

**SWITCHING ANTIPSYCHOTICS IN BIPOLAR DISORDER**

As with the treatment of schizophrenia, the process of switching antipsychotics must be done carefully when treating patients with bipolar disorder with due consideration given to the pharmacokinetics of the drugs involved. The use of multiple drugs is frequent in the treatment of bipolar disorder, and most of this polypharmacy is not evidenced-based. However, there is some preliminary evidence that mood stabilizers may ameliorate relapse rates consequent upon antipsychotic withdrawal. Lithium in particular may have a protective effect, reducing the rate of manic relapse when an atypical antipsychotic is withdrawn.

In general, the process of switching antipsychotic medications in bipolar disorder follows the same principles and protocols as in schizophrenia, although the clinician will have to be cognizant of specific factors related to this diagnosis. As outlined above, crucial considerations are the phase of treatment (mania/depression/maintenance) and any other medications that the patient is taking. Lithium, for example, is associated with a pronounced discontinuation syndrome and toxicity that may occur at normal serum levels, both of which may complicate switching to antipsychotics.

**CONCLUSION**

Antipsychotics are increasingly used in bipolar disorder as antimanic, antidepressant, and maintenance treatments. Although the clinical issues related to antipsychotics and switching are similar between schizophrenia and bipolar disorder, there are issues specific to bipolar disorder that must be attended to if the clinician is to be a “true apothecary.”

**Drug names:** haloperidol (Haldol and others), lithium (Eskalith, Lithobid, and others), olanzapine (Zyprexa).

**Disclosure of off-label usage:** The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents that is outside U.S. Food and Drug Administration–approved labeling has been presented in this article.

**REFERENCES**