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## DRUG INTERACTIONS IN THE TREATMENT OF BIPOLAR DISORDER

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Bipolar disorders are characterized by many different forms and episodes, which require specific pharmacological treatments. For the treatment or prevention of manic episodes, lithium salts, some atypical antipsychotic drugs and some anticonvulsants were introduced. Antidepressant drugs but also a very limited number of anticonvulsants (lamotrigine) and antipsychotic drugs (quetiapine) are recommended for the treatment of depressive episodes. In addition, benzodiazepines or related compounds may be useful as comedications for sleep problems or for their sedative properties. Polypharmacy is therefore rather common, also in case of insufficient response to a single drug, when the administration of a combination of active agents appears to be promising.

Most of these drugs are substrates of cytochrome P-450, and many of them are also either inducers or inhibitors of some of its isozymes. Interactions may also occur at the level of conjugating enzymes. Increasingly, knowledge about the underlying mechanisms of drug transport from intestine to the blood, and from the blood to the brain helps to predict interactions at this level. Indeed, many drugs are transported by P-glycoprotein, and inhibitors and inducers, respectively, may modify the transport of psychotropic drugs. Therefore, it is recommended to consider the interaction profile of each drug before initiating a combined treatment and adapt medication. Sometimes, despite it is known that interactions may occur with pharmacodynamic consequences, some risky combined treatments may nevertheless be useful. In such situations, careful titration of the drug doses and therapeutic drug monitoring are recommended.