Conventional IV chemotherapy regimens used for induction chemotherapy or salvage therapy in the treatment of multiple myeloma (MM) are cumbersome, with a negative impact on patient quality of life. A number of new oral drugs, including immunomodulatory agents such as thalidomide and lenalidomide, have demonstrated potent antimyeloma activity in relapsed and refractory as well as newly diagnosed MM. Clinically, response rates of 56%–72% have been reported with the combination of thalidomide and dexamethasone in patients with newly diagnosed disease; however, the combination is associated with a higher incidence of side effects, including constipation, somnolence, peripheral neuropathy, and thromboembolic complications. In contrast, preliminary safety and efficacy data from clinical studies of lenalidomide show promise. Response rates as high as 83% have been reported in patients with newly diagnosed MM, and the most common adverse event is manageable myelosuppression, which is reversible with dose reduction. Lenalidomide has different toxicities than thalidomide, exhibiting greater myelosuppression but virtually no constipation, somnolence, or peripheral neuropathy. Oncology nurses play a key role in monitoring patients for side effects and pain control and educating them about emerging treatment options. This article reviews the nursing experience with oral agents in the treatment of MM.