Immunomodulating agents such as thalidomide and its newly emerged derivative, lenalidomide, are becoming increasingly popular in the treatment of multiple myeloma because of their ability to combat drug resistance. Clinical trials suggest that thalidomide and lenalidomide are effective in all stages of multiple myeloma treatment—new diagnoses, stem cell transplantations, maintenance therapy, and relapsed or refractory disease. The drugs are most efficacious when combined with additional chemotherapeutic agents and/or corticosteroids. However, deep vein thrombosis and other thromboembolic events are associated with the treatment regimens. Oncology nurses must understand the pharmacologic properties of the drugs and the potentially life-threatening complications associated with them. To provide the highest standard of care, oncology nurses must play a vital role in the prevention, diagnosis, and management of thromboembolic events through awareness of the clinical problem, assessment tools, and thromboembolic prophylactic regimens.