Poor drug delivery to lesions in patients’ eyes is a major obstacle to the treatment of ocular diseases. The accessibility of these areas to drugs is highly restricted by the presence of barriers, including the corneal barrier, aqueous barrier, and the inner and outer blood–retinal barriers. In particular, the posterior segment is difficult to reach for drugs because of its structural peculiarities. This review discusses various barriers to drug delivery and provides comprehensive information for designing nanoparticle-mediated drug delivery systems for the treatment of ocular diseases. Nanoparticles can be designed to improve penetration, controlled release, and drug targeting. As highlighted in this review, the therapeutic efficacy of drugs in ocular diseases has been reported to be enhanced by the use of nanoparticles such as liposomes, micro/nanospheres, microemulsions, and dendrimers. Our recent data show that intravitreal injection of targeted liposomes encapsulating an angiogenesis inhibitor caused significantly greater suppression of choroidal neovascularization than did the injection of free drug. Recent progress in ocular drug delivery systems research has provided new insights into drug development, and the use of nanoparticles for drug delivery is thus a promising approach for advanced therapy of ocular diseases.