immunosuppression, which includes a calcineurin inhibitor (cyclosporine or tacrolimus), corticosteroids, and antiproliferative immunosuppression (azathioprine, mycophenolate mofetil, sirolimus, or everolimus), is now the standard combination used. The combination immunosuppression strategy that is most commonly used and that achieves the best standard outcomes includes tacrolimus, mycophenolate mofetil, and prednisone. In those at high risk for rejection (multiparous women, sensitized individuals) or in situations where use of calcineurin inhibitors needs to be delayed (renal dysfunction), induction therapy using monoclonal (basiliximab) or polyclonal antibodies (antithymocyte globulin) to provide augmented immunosuppression is used. Over several months, as surveillance endomyocardial biopsies are regularly performed and clinical as well as subclinical pathologic quiescence is established, gradual weaning of steroids is undertaken. **Table 260-2** describes the immunosuppression drugs in common use.

TABLE 260-2 Immunoprophylaxis Drugs in Cardiac Transplantation

DRUG CLASS	GENERIC DRUG	CELLULAR TARGET	MAJOR SIDE EFFECTS
Calcineurin inhibitors	Cyclosporine	Binds to cyclophilin, which then inhibits calcineurin	Hypertension, dyslipidemia, gum hypertrophy, hypertrichosis
	Tacrolimus	Binds to immunophilin FK506 binding protein, which inhibits calcineurin	Hypertension, dyslipidemia, alopecia, diabetes mellitus
Antithymocyte globulin (ATG)	Rabbit ATG	T-cell depletion in blood and peripheral lymphoid tissues through complement-dependent lysis and T-cell activation and apoptosis	Cytokine release syndrome, leukopenia, thrombocytopenia, serum sickness
	Horse ATG	Same as above	Same as above
Interleukin-2 receptor antagonists	Basiliximab	Inhibition of CD-25 of interleukin 2 receptor	Well tolerated; rare hypersensitivity; increased infection risk if used with calcineurin inhibitors
Antimetabolites	Azathioprine	Imidazolyl derivative and prodrug of 6-mercaptopurine (cell cycle inhibitor)	Bone marrow suppression, pancreatitis, hepatitis
	Mycophenolate Mofetil	Inhibits inosine monophosphate dehydrogenase, which controls guanine monophosphate in the de novo pathway of purine synthesis (inhibits T- and B-cell proliferation)	Leukopenia, gastrointestinal toxicity
Proliferation signal inhibitors	Sirolimus	Binds with FKBP12 and complex inhibits the mechanistic target of rapamycin (mTOR)	Delayed wound healing, nonspecific pneumonia, pericardial effusion, hyperlipidemia (hypertriglyceridemia)
	Everolimus	Binds to FKBP12, which inhibits mTORC1 (and not mTORC2)	Dyslipidemia, stomatitis, pericardial effusions, and pancytopenia

Acute cellular rejection (ACR) and antibody-mediated rejection (AMR) are two separate forms of cardiac allograft rejection that are recognized and can sometimes coexist. ACR occurs early after transplantation and then tends to decline in incidence after 6 months. This occurs due to a T cell–mediated assault on the donor allograft tissue and histologically is characterized by lymphocytic infiltrates in