A rectangular waveguide filled with a uniaxial medium is treated. Different orientations of the optic axis are considered, and the transmission characteristics of the guided waves are studied. When the optic axis is parallel to one of the x-, y-, and z-axes, results of wave decompositions with respect to the optic axis are presented and compared with conventional transverse-to-z solutions. Computation shows that the anisotropy not only changes the field distributions, but also leads to changes in the dominant modes in the waveguide. When the optic axis is tilted but lying in one of the sidewall planes, TE_{0n} or TE_{m0} (to z) modes are shown to exist, and supported hybrid wave modes are found from calculations using the proposed boundary condition matrix method. The hybrid wave is expressed as a linear combination of ordinary and extraordinary waves. The algorithm developed to address this problem is illustrated and numerical examples are given. The validity of the solution is verified by comparing its results with those of the aligned cases that are analytically solved.