The antiepileptic activity of α-substituted acetamides, lactams, and cyclic imides has been known for over six decades. We recently proposed an α-substituted amide group as the minimum pharmacophore responsible for inhibition of neuronal nicotinic acetylcholine receptors by these compounds, with the implication that inhibition of these receptors in the brain might be the unifying mechanism of action for these classes of antiepileptic drugs. In order to realize the pharmacological potential of these orally administered drugs, the relevant aspects of solid-state chemistry and pharmaceutics (including solubility and stability) need to be addressed. A better - more cohesive and generalized - understanding of the solid-state properties of these drugs would pave the road for a rational approach to their development, formulation, and manufacturing. In this paper, Pharmaceutically relevant aspects of the crystal structure and solid-state chemistry of antiepileptic drugs containing the α-substituted amide bond pharmacophore - α-substituted acetamides, lactams, and cyclic imides and the structurally related barbiturates, hydantoins, and acetylureas are reviewed. The applicable experimental and computational approaches are also briefly mentioned.