Active pharmaceutical ingredients in most drugs are present as crystalline forms. It is imperative to accurately characterize the crystal structure of API because the molecular arrangements in a crystal can largely determine physical and chemical properties, which in turn influence the processing and formulation of pharmaceutical solids, as well as key drug properties such as dissolution rate and stability. However, many crystalline APIs cannot be prepared as single crystals of suitable size and quality to be used in single crystal X-ray diffraction. In such cases, powder X-ray diffraction techniques can be applied to probe the crystal structures of novel crystalline pharmaceutical molecules. Recent developments in both instrumentation and computing strategies have enabled \textit{ab-initio} structure determination from PXRD to become a common practice. In this work, the structure determination procedures of small molecule drug compounds will be described. In addition, other important areas of PXRD applications in drug development will be highlighted.