CRYSTAL STRUCTURES OF LARGE-VOLUME COMMERCIAL PHARMACEUTICALS

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As part of a continuing project, the challenging room-temperature crystal structures of eight commercial pharmaceutical APIs have been solved by Monte Carlo simulated annealing techniques using synchrotron X-ray powder diffraction data (11-BM at APS), and optimized using density functional techniques. **Tofacitinib dihydrogen citrate (Xeljanz®)**, $(C_{15}H_{21}N_6O)(H_2C_6H_5O_7)$, crystallizes in $P2_12_12_1$ with a = 5.91113(1), b = 12.93131(3), c = 30.43499(7) Å, V = 2326.411(6) Å^3, and Z = 4. All of the "interesting" hydrogn atoms could be located by analysis of potential hydrogen bonding patterns. **Eltrombopag olamine Form I (Promacta®)**, $(C_2H_8NO)_2(C_{25}H_{20}N_4O_4)$ crystallizes in $P2_1/n$ with a = 17.65884(13), b = 7.55980(2), c = 22.02908(16) Å, $\hat{a}$ = 105.8749(4)E, V = 2828.665(11) Å^3, and Z = 4. The initial structure solution reversed the orientation of one of the cations. **Levocetirizine hydrochloride Form I (Zyzal)**, $C_{21}H_{27}ClN_2O_3Cl$, apparently crystallizes in $P2_1/n$ (even though it is a chiral molecule and exhibits weak second-harmonic generation) with a = 24.1318(21), b = 7.07606(9), c = 13.5205(7), $\hat{a}$ = 97.9803(4)E, V = 2286.38(12) Å^3, and Z = 4.

Edoxaban tosylate monohydrate Form I (Lixiana®), $(C_{24}H_{31}ClN_7O_4S)(C_7H_7O_3S)(H_2O)$, crystallizes in $P2_1$ with a = 7.55097(2), b = 7.09010(2), c = 32.08420(21) Å, $\hat{a}$ = 96.6720(3)E, V = 1744.348(6) Å^3, and Z = 2. **Tezacaftor Form A (Symdeko)**, $C_{26}H_{27}F_3N_2O_6$, crystallizes in $C2$ with a = 21.05142(2), b = 6.60851(2), c = 17.76032(5) Å, $\hat{a}$ = 95.8255(2)E, V = 2458.027(7) Å^3, and Z = 4. **Pomalidomide Form I (Pomalyst)**, $C_{13}H_{11}N_3O_4$, crystallizes in $P\text{-}1$ with a = 7.04742(9), b = 7.89103(27), c = 11.3106(6) Å, $\acute{a}$ = 73.2499(13), $\hat{a}$ = 80.9198(9), $\tilde{a}$ = 88.5969(6)E, V = 594.618(8) Å^3, and Z = 2. **Palbociclib isethionate Form B (Ibrance®)**, $(C_{24}H_{30}N_7O_2)(C_2H_5O_4S)$, crystallizes in $P\text{-}1$ with a = 8.71337(4), b = 9.32120(6), c = 17.73722(20) Å, $\acute{a}$ = 80.0258(5), $\hat{a}$ = 82.3581(3), $\tilde{a}$ = 76.1560(2)E, V = 1371.284(5) Å^3, and Z = 2. **Osimertinib mesylate Form B (Tagrisso)**, $(C_{28}H_{34}N_7O_2)(CH_3O_3S)$ crystallizes in $P\text{-}1$ with a = 11.4291(3), b = 11.7223(4), c = 13.3221(4), $\acute{a}$ = 69.0246(8), $\hat{a}$ = 74.5906(7), $\tilde{a}$ = 66.4001(7)E, V = 1511.466(13) Å^3, and Z = 2. Other new structures may be discussed as they become available.

Keywords: pharmaceutical, powder diffraction, Rietveld refinement, density functional theory