

Beyond Rule of Five (bRo5) Orally Active Pharmaceuticals

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|----|---------------------|----|-----------------------------|----|---------------------|----|----------------------|----|-----------------------------|----|---------------------------|----|----------------------|----|--------------------|----|-------------------------|----|--------------------------------------|----|-----------------------|----|---|----|---------------------|
| 1 | Cyclosporine | 2 | Pibrentasvir | 3 | Desmopressin | 4 | Everolimus | 5 | Siroliimus | 6 | Ombitasvir | 7 | Ledipasvir | 8 | Velpatasvir | 9 | Elbasvir | 10 | Flurithromycin ethylsuccinate | 11 | Rifapentine | 12 | Ivermectin | 13 | Voxilaprevir |
| 14 | Venetoclax | 15 | Rifaximin | 16 | Glecaprevir | 17 | Dirithromycin | 18 | Rokitamycin | 19 | Rifampin | 20 | Telithromycin | 21 | Tacrolimus | 22 | Digoxin | 23 | Vinorelbine | 24 | Cobicistat | 25 | Grazoprevir | 26 | Paritaprevir |
| 27 | Vaniprevir | 28 | Simeprevir | 29 | Azithromycin | 30 | Asunaprevir | 31 | Clarithromycin | 32 | Daclatasvir | 33 | Erythromycin | 34 | Ritonavir | 35 | Itraconazole | 36 | Atazanavir | 37 | Posaconazole | 38 | Lomitapide | 39 | Telaprevir |
| 40 | Saquinavir | 41 | Naloxegol | 42 | Amiodarone | 43 | Moxidectin | 44 | Dabigatran Etexilate | 45 | Lercanidipine | 46 | Manidipine | 47 | Tipranavir | 48 | Elexacaftor | 49 | Lusutrombopag | 50 | Etoposide | 51 | Montelukast | 52 | Brigatinib |
| 53 | Lapatinib | 54 | Netupitant | 55 | Zafirlukast | 56 | Letermovir | 57 | Midostaurin | 58 | Eluxadoline | 59 | Nelfinavir | 60 | Fosinopril | 61 | Thiocolchicoside | 62 | Atorvastatin | 63 | Ceritinib | 64 | Dronedaron | 65 | Omadacycline |
| 66 | Bedaquiline | 67 | Gilteritinib | 68 | Alisikiren | 69 | Bosentan | 70 | Edoxaban | 71 | Encorafenib | 72 | Delamanid | 73 | Nilotinib | 74 | Sofosbuvir | 75 | Lumefantrine | 76 | Dutasteride | 77 | Fedratinib | 78 | Tezacaftor |
| 79 | Dabrafenib | 80 | Tenofovir Disoproxil | 81 | Telmisartan | 82 | Cefditoren | 83 | Dipyridamole | 84 | Adefovir Dipivoxil | 85 | Sarecycline | 86 | Leucovorin | 87 | Methotrexate | 88 | Folic Acid | 89 | Valganciclovir | | LIPINSKI'S RULE OF FIVE¹ Molecular Weight \leq 500 g/mol clogP \leq 5 Hydrogen Bond Donors (HBD) \leq 5 Hydrogen Bond Acceptors (HBA) \leq 10 (N+O) VEBER'S RULES² Topological Polar Surface Area (TPSA) \leq 140 Å ² Number of Rotatable Bonds (NRB) \leq 10 | | |

Key: Antimicrobial, Activa, Cardiovascular Disorders, Oncology, GI Disorders, Immunosuppressant, Respiratory Disorders, Anticancer, Misc

Restricted to small-molecule drugs that undergo oral absorption and fail >1 Lipinski rules. Prodrugs classified in the GI prior to absorption were excluded.

¹clogP determined as ALogP.

²Lipinski, C. A. et al. *Adv. Drug Deliv. Rev.* 1997, 33, 3–25.

³Veber, D. F. et al. *J. Med. Chem.* 2002, 45, 2615–2623.