

| Table 3. Pharmacokinetic and Pharmacodynamic Parameters of Opioids                               |                 |   |  |  |   |                                 |
|--|-----------------|---|--|--|---|---------------------------------|
| Medication (Brand Name)  | Schedule        | Clinical Considerations   |  | Decrease in Effect   | Increase in Effect  | MS Dose Equivalent <sup>a</sup> |
| <b>Buprenorphine (Belbuca, Butrans, Buprenex)</b>  | III             | Mu agonist, kappa antagonist<br>Improves mood<br>Possible QT prolongation<br>Lesser euphoria than other opioids <sup>17-19</sup><br>Lesser abuse potential<br>Poorly antagonized by naloxone<br>Suppresses hyperalgesia <sup>13,14</sup><br>Less immunosuppression<br>Less acute pain control |  | Nevirapine, modafinil, CYP-450 3A4 inducers, and universal inducers <sup>b</sup>                           | Itself and ketoconazole, nefazodone, fluvoxamine, ritonavir, erythromycin, grapefruit juice, other 3A4 inhibitors; as well as methadone and fentanyl      | 30:1                            |
| <b>Codeine (generic)</b>   | II <sup>c</sup> | Prodrug of hydromorphone and morphine<br>Poor pain control property   |  | Paroxetine, fluoxetine, duloxetine, and other CYP-450 2D6 inhibitors                                       | Rifampin, dexamethasone, other 2D6 inducers and universal inducers; <sup>b</sup> as well as tramadol and hydrocodone                                      | 1:10                            |
| <b>Fentanyl (Abstral, Actiq, Duragesic, Fentora, Onsolis, generic)</b>                           | II              | Less constipation and less GI spasm <sup>15,16</sup>  |  | Ketoconazole, nefazodone, fluvoxamine, ritonavir, erythromycin, grapefruit juice, and other 3A4 inhibitors | Nevirapine, modafinil, other 3A4 inducers, and universal inducers; <sup>b</sup> as well as by methadone and buprenorphine                                 | 70-100:1                        |
| <b>Hydrocodone (generic)</b>   | II              | Prodrug of hydromorphone and morphine<br>Powerful euphoria<br>Consider dosage of acetaminophen in combination products  |  | Paroxetine, fluoxetine, duloxetine, and other 2D6 inhibitors   | Rifampin, dexamethasone, other 2D6 inducers and universal inducers; <sup>b</sup> as well as tramadol and codeine  | 1.2:1                           |
| <b>Hydromorphone (Dilaudid, Exalgo, generic)</b>   | II              | Less constipation<br>Powerful euphoria  |  | Carbamazepine, phenytoin, rifampin, phenobarbital, tobacco, and universal inducers <sup>b</sup>            |   | 8:1                             |
| <b>Levorphanol (generic)</b>   | II              | NMDA antagonism<br>5HT and NE reuptake inhibitor  |  | Carbamazepine, phenytoin, rifampin, phenobarbital, tobacco, and other universal inducers <sup>b</sup>      | TCAs, promethazine, ranitidine  | 7:1                             |
| <b>Meperidine (Demerol, generic)</b>   | II              | Structurally similar to atropine<br>Primarily kappa agonist<br>Anticholinergic, Na channels inhibitor<br>NE and dopamine reuptake inhibitor<br>Serotonin syndrome<br>Seizures   |  | Carbamazepine, phenytoin, rifampin, phenobarbital, tobacco, and other universal inducers <sup>b</sup>      |   | 1:10                            |
| <b>Methadone (Dolophine, Methadose, generic)</b>   | II              | Never use PRN due to unpredictable half-life <sup>20-21</sup><br>Long acting, but short-lived pain control<br>NMDA antagonism<br>QT prolongation<br>Higher incidence of encephalopathy  |  | Carbamazepine, phenytoin, rifampin, phenobarbital, tobacco, and other universal inducers <sup>b</sup>      | Itself, ketoconazole, nefazodone, fluvoxamine, ritonavir, ketoconazole, erythromycin, grapefruit juice, other 3A4 inhibitors, fentanyl, and buprenorphine | Nonlinear                       |
| <b>Morphine (Astromorph PF, Duramorph PF, Infumorph, Kadian, Morphabond, MS Contin, generic)</b> | II              | 75% metabolized into toxic M3G, the rest into codeine and hydromorphone   |  | Carbamazepine, phenytoin, rifampin, phenobarbital, tobacco, and other universal inducers <sup>b</sup>      | TCAs, promethazine, ranitidine  | 1:1<br>"Gold standard"          |
| <b>Oxycodone (OxyContin, Oxaydo, Roxicodone, Xtampza ER, generic)</b>                            | II              | More potent kappa than mu agonist<br>Powerful euphoria<br>At higher doses, greater incidence of encephalopathy  |  | Rifampicin, dexamethasone, and other 2D6 inducers; universal inducers <sup>b</sup>                         | Paroxetine, fluoxetine, duloxetine, and other 2D6 inhibitors  | 1.5:1                           |
| <b>Oxymorphone (Opana, Opana ER, generic)</b>  | II              | Less sedation<br>Fewer seizures<br>Take on empty stomach as food increases T <sub>max</sub><br>Misoprostol interferes with absorption   |  | Carbamazepine, phenytoin, rifampin, phenobarbital, tobacco, and other universal inducers <sup>b</sup>      |   | 5:1                             |
| <b>Tapentadol (Nucynta, Nucynta ER)</b>  | II              | Mu agonist and NE reuptake inhibitor<br>No active metabolites<br>May cause serotonin syndrome, hallucinations, and seizures.  |  | Carbamazepine, phenytoin, rifampin, phenobarbital, tobacco, and other universal inducers <sup>b</sup>      |   | 1:5                             |
| <b>Tramadol (Rybix, Ryzolt, Ultram, Ultram ER, generic)</b>                                      | IV              | Prodrug<br>Mu agonist and 5HT reuptake inhibitor<br>May cause serotonin syndrome and seizures   |  | Paroxetine, fluoxetine, duloxetine, and other 2D6 inhibitors   | Rifampin, dexamethasone, other 2D6 inducers; universal inducers <sup>b</sup>  | 1:5                             |

CYP-450, cytochrome P 450; GI, gastrointestinal; 5HT, serotonin; MAOI, monoamine oxidase inhibitor; Na, sodium; NE, norepinephrine; NMDA, N-methyl-D-aspartate; PRN, as required; TCA, tricyclic antidepressant

<sup>a</sup> Relative potency and dose equivalency varies depending on sources; there are no universally accepted parameters

<sup>b</sup> Universal inducers of P-450: carbamazepine, phenytoin, rifampin, phenobarbital, tobacco

<sup>c</sup> Schedule III when lower dose is used in combination medications

DO NOT COMBINE opioids with benzodiazepines and alcohol.

AVOID use in combination with sedating medications.

AVOID use in brain trauma and increase in intracranial pressure.

AVOID use in gastroparesis, ileus, spastic colon, sphincter of Oddi, and biliary system spasm.

AVOID chronic use in patients with addiction risk factors.

AVOID use in headaches.

AVOID use in bradyarrhythmias and severe orthostatic hypotension.

AVOID use in urinary retention, severe constipation, severe prostate enlargement, and closed angle glaucoma.

AVOID use in hypoxia, hypercapnia, and chronic pulmonary disease.

PREGNANCY: Use buprenorphine or methadone if use cannot be avoided.