Astronauts use medications for the treatment of a variety of illnesses during space travel. Data mining efforts to assess minor clinical conditions occurring during Shuttle flights STS-1 through STS-94 revealed that space motion sickness (SMS) was the most common ailment during early flight days, occurring in ~40% of crewmembers, followed by digestive system disturbances (9%) and infectious diseases, which most commonly involved the respiratory or urinary tracts. A more recent analysis of postflight medical debriefs data to examine trends with respect to medication use by astronauts during spaceflights indicated that ~37% of all prescriptions recorded was for pain followed by sleep (22%), SMS (18%), decongestion (14%), and all others (14%). Further analysis revealed that about 150 of 317 crewmembers experienced symptoms of SMS. Nearly all (132 of 150) crewmembers took medication for the treatment of symptoms with a total of 387 doses. Promethazine was taken most often (201 doses); in most cases this resulted in alleviation of symptoms with 130 crewmembers (65%) reporting feeling much or somewhat better. Although fewer total doses of the combination of promethazine and dextroamphetamine (Phen/Dex) were taken (45 doses), slightly more than half of these doses resulted in improvement. The combination of scopolamine and dextroamphetamine (Scop/Dex) was reported to be effective in only 37% of cases, with 36 of 97 total doses resulting in improvement. A higher percentage (24%) of Scop/Dex doses was reported to be ineffective compared with promethazine alone or as Phen/Dex (10% and 7%, respectively). Comparisons of the effectiveness of the different dosage forms of promethazine revealed that intramuscular injection was most effective in alleviating symptoms with 55% feeling much better, 16% feeling somewhat better, and only 7% feeling no effect or worse. Overall, it appears that promethazine alone was used more frequently during flight and was reported effective for the treatment of SMS.