b. Classes of drugs

Drugs can be classed by the *Anatomical Therapeutic Chemical* (ATC) system (20,21,22,23,24). This system is based on the assumption that compounds with similar physical and chemical properties exhibit similar biological activities (25). Lin et al. (26) describe the utility of the ATC system, and also identify a number of databases that list drugs, their associated adverse events, and drug targets. One such database is Drugbank, available from the University of Alberta. Drugdex®, provided by Thomson Reuters, is another database on dosage, pharmacokinetics, indications, and adverse drug reactions. The ATC system, as well as the listed databases, can aid in drafting package inserts.

c. Black box warning

Where a drug presents a serious risk that can lead to death or serious injury, the FDA may require that the package insert include a black box warning. This warning informs the physician that patients taking the drug need to be closely monitored (27). Black box warnings include those that require laboratory testing, avoiding other drugs (warning regarding drug/drug interactions), avoiding prescribing in the presence of another specified health condition, or knowing the risks associated with a specific population, such as pregnant women.

Black box warnings take the form of a writing that resides inside of a black box. Examples appear below. These examples, which are from drugs discussed earlier in this book, include an anti-cancer drug (cisplatin), an anti-viral drug (ribavirin), and an anti-depressant (Zoloft®).

The black box warning for cisplatin (28) reads:

[20] Takarabe M, Shigemizu D, Kotera M, Goto S, Kanehisa M. Characterization and classification of adverse drug interactions. *Genome Inform*. 2010;22:167–175.

[21] Imming P, Sinning C, Meyer A. Drugs, their targets and the nature and number of drug targets. *Nat Rev Drug Discov*. 2006;5:821–834.

[22] Bender A, Scheiber J, Glick M, et al. Analysis of pharmacology data and the prediction of adverse drug reactions and off-target effects from chemical structure. *ChemMedChem*. 2007;2:861–873.

[23] Imming P, Buss T, Dailey LA, et al. A classification of drug substances according to their mechanism of action. *Pharmazie*. 2004;59:579–589.

[24] Gurulingappa H, Kolárik C, Hofmann-Apitius M, Fluck J. Concept-based semi-automatic classification of drugs. *J Chem Inf Model*. 2009;49:1986–1992.

[25] Dunkel M, Günther S, Ahmed J, Wittig B, Preissner R. SuperPred: drug classification and target prediction. *Nucleic Acids Res*. 2008;36:W55–W59.

[26] Lin SF, Xiao KT, Huang YT, Chiu CC, Soo VW. Analysis of adverse drug reactions using drug and drug target interactions and graph-based methods. *Artif Intell Med*. 2010;48:161–166.

[27] Ricci JR, Coulen C, Berger JE, Moore MC, McQueen A, Jan SA. Prescriber compliance with black box warnings in older adult patients. *Am J Manag Care*. 2009;15:e103–e108.

[28] Package insert. Bedford Laboratories, Cisplatin injection, (June 2004).