PART A  LIFECYCLE MANAGEMENT BUSINESS ENVIRONMENT  

1. Challenges Facing the Branded Drug Industry  
    1.1 Depleted NME Pipelines/Lower R&D Efficiency  
    1.2 Higher Development Costs  
    1.3 Safety Concerns  
    1.4 Tougher Environment for Pricing, Reimbursement, and Listing  
    1.5 Increased Competition  
    1.6 Earlier Genericization  
    1.7 Faster Sales Erosion Following Patent Expiry  
    1.8 Poor Image of Branded Drug Industry  
    1.8.1 Prosperity of the Branded Drug Industry  
    1.8.2 Lack of Innovation  
    1.8.3 Marketing Spend and Tactics  
    1.8.4 Safety Issues  
    1.8.5 Keeping Generics Off the Market  
    1.9 Diversification  

2. The Life Cycle of Industries, Technologies, and Brands  
    2.1 Diffusion of Innovations  
    2.2 The Lifecycle Curve  
    2.3 Lifecycle Phases  
    2.3.1 Development Phase  
    2.3.2 Introduction Phase  
    2.3.3 Growth Phase  
    2.3.4 Maturity Phase  
    2.3.5 Decline Phase
3. The Life Cycle of a Pharmaceutical Brand

3.1 Lifecycle Curve of Pharmaceuticals
   3.1.1 Slow Rate of Growth during the Growth Phase
   3.1.2 Lack of a True Maturity Phase
   3.1.3 Precipitous Decline Phase

3.2 Factors Affecting Rate of Conversion to Generics
   3.2.1 Government Policy
   3.2.2 Disease
   3.2.3 Size of Brand
   3.2.4 Hospital versus Nonhospital Drug Usage
   3.2.5 Active Substance and Other Barriers to Entry

3.3 The Life Cycle of a Pharmaceutical Brand

PART B LIFECYCLE MANAGEMENT REGULATORY AND LEGAL ENVIRONMENT

4. The Generic Approval Process
   4.1 United States
   4.2 Europe
   4.3 Japan

5. Hatch–Waxman Legislation and Its Effects on LCM
   5.1 Hatch–Waxman Act of 1984
   5.2 Medicare Modernization Act of 2003
   5.3 FDA Amendments Act of 2007
   5.4 Q1 Program Supplemental Funding Act of 2008
   5.5 Discussion of Hatch-Waxman Legislation

6. U.S. Health-Care Reform 2010

7. European Sector Inquiry

PART C PATENTS AND EXCLUSIVITIES

8. Patents and Other Intellectual Property Rights
   8.1 Nonpatent Intellectual Property Rights
   8.2 What Are Patents?
   8.3 What Is Patentable?
      8.3.1 Patentable Subject Matter
      8.3.2 Novelty
8.3.3 Inventive Step 85
8.3.4 Utility 86
8.3.5 Disclosure 86
8.4 How Long Does a Patent Last? 87
8.5 Patent Term Restoration in the United States 87
8.6 Supplementary Protection Certificates in Europe 88
8.7 Patent Term Extension in Japan 89
8.8 How Are Patents Obtained? 89
8.9 Patent Enforcement 91
8.10 Types of Patents 92
  8.10.1 Composition of Matter Patent 93
  8.10.2 Medical Use Patent 93
  8.10.3 Formulation Patent 94
8.11 KSR versus Teleflex—Raising the Nonobviousness Bar 94
8.12 Patent Strategy 96

9. Nonpatent Exclusivities 99
  9.1 NCE Exclusivity (United States) 99
  9.2 New Clinical Study Exclusivity (United States) 100
  9.3 Data and Marketing Exclusivity (Europe) 100
  9.4 Data Exclusivity (Japan) 101
  9.5 Orphan Drug Exclusivity 101
  9.6 Pediatric Exclusivity 103
  9.7 180-Day Generic Product Exclusivity 105


PART D DEVELOPMENTAL LCM 113

11. Strategic Principles of Developmental LCM 115
  11.1 Developmental LCM Goal 1: Provide a Meaningful Improvement in Clinical Profile 116
  11.2 Developmental LCM Goal 2: Increase the Potential Real-World Patient Potential for the Brand 118
  11.3 Developmental LCM Goal 3: The Ability to Generate an ROI 120
  11.4 Developmental LCM Goal 4: The Ability to Enhance Market Exclusivity of the Brand Franchise 121

12. Indication Expansion and Sequencing 123
  12.1 Categories of Indication Expansion 123
13. Patient Subpopulations and Personalized Medicine

13.1 What Does a Good Patient Selection Strategy Look Like?

13.2 Patient Selection without Predictive Criteria: Post Hoc Approaches

13.3 What about the Patients Who Are Not Selected?

14. New Dosage Strengths, New Dosage Regimens

14.1 New Dosage Strengths

14.2 New Dosage Regimens

15. Reformulation, New Routes of Administration, and Drug Delivery

15.1 Reformulation and New Routes of Administration

15.1.1 Switch and Grow Strategy

15.1.2 Expand and Grow Strategy

15.1.3 Generic Defense

15.2 Drug Delivery Devices

16. Fixed-Dose Combinations (FDCs) and Co-Packaging

17. Second-Generation Products and Modified Chemistry

17.1 Isomerism

17.2 Polymorphism

17.3 Salts, Ethers, and Esters

17.4 Prodrugs and Metabolites

18. Other Developmental LCM Strategies

18.1 Manufacturing Strategies

18.2 White Papers and Citizen Petitions

PART E COMMERCIAL LCM

19. Strategic Principles of Commercial LCM

19.1 Commercial LCM Goal 1: The Ability to Drive Widespread and Preferential Patient Access to the Brand

19.2 Commercial LCM Goal 2: The Ability to Defend Market Access and Formulary Position

19.3 Commercial LCM Goal 3: The Ability to Optimize Profitability of the Brand Franchise
20. Geographical Expansion and Optimization 172
  20.1 Geographic Expansion 174
  20.2 Harmonization and Rationalization 175

21. OTC Switching 178
  21.1 What to Switch: Choosing the Best Approach 179
  21.2 Where to Switch: Dealing with Intermarket Variability 181
  21.3 When to Switch: Balancing the Product Life Cycle? 183
  21.4 How to Make the Switch Successful: What Corporate Support Is Required? 184

22. Brand Loyalty and Service Programs 186

23. Strategic Pricing Strategies 190
  23.1 Pricing Strategy and Tactics in the Launch and Growth Phases 190
  23.2 Pricing Strategy and Tactics Following Patent Expiry 193

24. Generic Strategies and Tactics 198
  Building a Generic Portfolio: Old versus New Thinking 202

25. Exit Strategies 204
  Executing the Exit Strategy 206

PART F BIOLOGICS AND BIOSIMILARS 207

26. Biologics and LCM 209
  26.1 Emergence of Biotech 209
  26.2 Some Definitions 210
    26.2.1 Biologics 210
  26.3 Uptake and Value of Biologics 211
  26.4 LCM of Biologics 213
    26.4.1 Next-Generation Biologics 213
    26.4.2 Reformulation 214
    26.4.3 Indication Expansion 215
    26.4.4 Self-Injection Devices 215

27. Biosimilars and Their Impact on Biologic LCM 217
  27.1 Changing Terminology: Biogenerics, Biosimilars, and FOBs 217
  27.2 Why Are Biosimilars a Big Deal? 219
27.3 How Are Biosimilars Different? 220
27.4 Biosimilar Approval Pathways 220
27.4.1 Biosimilars in Europe 220
27.4.2 Biosimilars in the United States 221
27.4.3 Biosimilars around the World 222
27.5 Substitution of Biosimilars 223
27.5.1 Automatic Substitution 223
27.5.2 Therapeutic Substitution 224
27.6 Innovator Responses to Biosimilar Threats 225
27.7 The Future for Biologics LCM 226
27.7.1 Legal Strategies in the United States 227
27.7.2 Indication Expansion in Europe 228
27.7.3 Brand Loyalty Programs and Services 229
27.8 The Emergence of the “Innovasimilar” Biopharma Company 229
27.9 Final Words 231

PART G THE INTEGRATED BRAND LCM STRATEGY AND ITS IMPLEMENTATION 233

28. Strategic Goals of LCM Brand Plans 235
28.1 Position to Market 235
28.2 Comparative Clinical Profile versus Gold Standard 237
28.3 Level of Market Unmet Need 237

29. Ten Keys to Successful LCM 238
29.1 Excellent Functional Expertise 238
29.1.1 Patent Attorneys 239
29.1.2 Regulatory Affairs 240
29.1.3 Clinical Development 240
29.1.4 Formulation Scientists 241
29.1.5 Marketing and Sales 242
29.1.6 Manufacturing 243
29.2 Visible Management Support 244
29.3 Unambiguous Ownership 245
29.4 An Early Start 246
29.5 A Robust “Broad to Bespoke” Process 248
29.6 Focus on “High LCM Value Brands” 249
29.7 Adequate Resources 250
29.8 Measurements and Rewards 250
29.9 Training and Support 252
29.10 Realism 252
30. Organizational Structures and Systems for Ensuring Successful LCM 254

30.1 Organization of Project and Brand Management 254
   30.1.1 Functional Structure 255
   30.1.2 Project Structure 255
   30.1.3 Matrix Structure 257
30.2 Project and Brand LCM Structures 259
30.3 LCM Center of Excellence 263
30.4 Composition of the LCM CoE 266

31. The LCM Process: Description, Timing, and Participants 268

31.1 Purpose of the LCM Process 268
31.2 Timing of the LCM Process 269
31.3 Description of the LCM Process 271

PART H INTEGRATING LCM WITH PORTFOLIO MANAGEMENT 277

32. Principles of Portfolio Management 279

33. LCM Projects in the Development Portfolio 284

34. Managing Established Brand Portfolios 286
   34.1 What Do You Do with a Priority Established Brand? 288
   34.2 What about the Nonpriority Brands? 289
   34.3 Building the Ideal Established Brands Portfolio 290

CONCLUSIONS 291

APPENDIX: CASE HISTORIES 294

A.1 Market and Product-Shaping Dynamics in Action 294
   Alzheimer’s Disease Therapies: Aricept®, Exelon®, and Reminyl®/Razadyne® 294
   Learnings 297
A.2 Optimizing Clinical Profile versus Gold Standards 298
   Angiotensin II Receptor Blockers (ARBs): Cozaar®, Micardis®, and Benicar® 298
   Learnings 299
A.3 Partnering to Ensure Reimbursement and Collection of Cost-Effectiveness Data 299
   Aricept 299
   Learnings 301
A.4 Active Metabolites and Late-Listed Patents 301
   Buspar® 301
   Learnings 303
A.5 A Fixed-Dose Combination (FDC) That Could Not Fail, or Could It? 303
   Caduet® 303
   Learnings 304
A.6 Indication Expansion 305
   Certican®/Zortress® and Afinitor® 305
   Learnings 306
A.7 Killing a Franchise through Over-the-Counter (OTC) Switching 307
   Claritin® 307
   Learnings 308
A.8 Moving FDCs to the Fore in Diabetes 308
   Diabetes Therapies: Glucophage®, Avandia®, Actos®, and Januvia® 308
   Learnings 310
A.9 FDCs and Multiple Dosage Strengths 310
   Diovan® and Tekturna®/Rasilez® 310
   Learnings 312
A.10 Building a Compliance Support Program 312
   Enbrel® 312
   Learnings 314
A.11 Targeting Responders with High-Price Cancer Agents 314
   Erbitux® 314
   Learnings 315
A.12 Failure of a “No-Brainer” LCM Strategy 315
   Exubera® 315
   Learnings 319
A.13 At-Risk Launches and Prodrug Patents 320
   Famvir® 320
   Learnings 321
A.14 New Dosages, FDC, and Patent Litigation 322
   Fosamax® 322
   Learnings 324
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.15</td>
<td>High Regulatory Hurdles for Lifestyle Drugs</td>
<td>325</td>
</tr>
<tr>
<td>Girosa®</td>
<td>325</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>327</td>
<td></td>
</tr>
<tr>
<td>A.16</td>
<td>Big Money from Orphan Indications</td>
<td>327</td>
</tr>
<tr>
<td>Gleevec®</td>
<td>327</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>329</td>
<td></td>
</tr>
<tr>
<td>A.17</td>
<td>Not Giving Up on a Controversial Brand</td>
<td>330</td>
</tr>
<tr>
<td>Iressa®</td>
<td>330</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>332</td>
<td></td>
</tr>
<tr>
<td>A.18</td>
<td>Expanding a Medical Aesthetics Franchise with an Ophthalmic Drug</td>
<td>332</td>
</tr>
<tr>
<td>Latisse®</td>
<td>332</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>334</td>
<td></td>
</tr>
<tr>
<td>A.19</td>
<td>Patent Expiry of the Biggest Drug Brand Ever</td>
<td>335</td>
</tr>
<tr>
<td>Lipitor®</td>
<td>335</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>336</td>
<td></td>
</tr>
<tr>
<td>A.20</td>
<td>Early Out-Licensing by Biotech: Take the Money and Run</td>
<td>336</td>
</tr>
<tr>
<td>Macugen®</td>
<td>336</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>338</td>
<td></td>
</tr>
<tr>
<td>A.21</td>
<td>Codevelopment and Comarketing Deals End in a Megamerger</td>
<td>338</td>
</tr>
<tr>
<td>Merck and Schering-Plough: Zetia®/Vytorin® and Claritin/Singulair®</td>
<td>338</td>
<td></td>
</tr>
<tr>
<td>Zetia/Vytorin</td>
<td>339</td>
<td></td>
</tr>
<tr>
<td>Claritin/Singulair</td>
<td>342</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>343</td>
<td></td>
</tr>
<tr>
<td>A.22</td>
<td>A Hugely Successful LLCM Switch Strategy: Business Needs and Reputational Issues Collide</td>
<td>344</td>
</tr>
<tr>
<td>Prilosec® and Nexium</td>
<td>344</td>
<td></td>
</tr>
<tr>
<td>The Facts</td>
<td>344</td>
<td></td>
</tr>
<tr>
<td>The Public Reaction</td>
<td>345</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>347</td>
<td></td>
</tr>
<tr>
<td>A.23</td>
<td>Combining Production Outsourcing with Settlement with a Generic Competitor</td>
<td>349</td>
</tr>
<tr>
<td>Nexium</td>
<td>349</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>351</td>
<td></td>
</tr>
<tr>
<td>A.24</td>
<td>Reformulating for Success in Osteoporosis</td>
<td>351</td>
</tr>
<tr>
<td>Osteoporosis Drugs: Fosamax, Actonel®, Boniva®, and Aclasta®</td>
<td>351</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>353</td>
<td></td>
</tr>
<tr>
<td>Topic</td>
<td>Page</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>------</td>
<td></td>
</tr>
<tr>
<td>A.25 Isomerism, Polymorphism, and Settlements</td>
<td>354</td>
<td></td>
</tr>
<tr>
<td>Plavix®</td>
<td>354</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>355</td>
<td></td>
</tr>
<tr>
<td>A.26 Payers versus Brand for Patient Selection</td>
<td>356</td>
<td></td>
</tr>
<tr>
<td>Plavix and Brilinta</td>
<td>356</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>357</td>
<td></td>
</tr>
<tr>
<td>A.27 Litigation Can Delay Generic Entry in the OTC Field Too</td>
<td>358</td>
<td></td>
</tr>
<tr>
<td>Prilosec OTC</td>
<td>358</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>359</td>
<td></td>
</tr>
<tr>
<td>A.28 Inconsistent Court Decisions Can Hurt Both Brand and Generic Companies</td>
<td>360</td>
<td></td>
</tr>
<tr>
<td>Protonix®</td>
<td>360</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>361</td>
<td></td>
</tr>
<tr>
<td>A.29 Holding on to an Antipsychotic Franchise</td>
<td>362</td>
<td></td>
</tr>
<tr>
<td>Risperdal®/Invega®</td>
<td>362</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>363</td>
<td></td>
</tr>
<tr>
<td>A.30 LCM Creates an Almost Immortal Brand</td>
<td>364</td>
<td></td>
</tr>
<tr>
<td>Voltaren®</td>
<td>364</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>365</td>
<td></td>
</tr>
<tr>
<td>A.31 LCM of a Women’s Health Franchise</td>
<td>366</td>
<td></td>
</tr>
<tr>
<td>The Yasmin® Family</td>
<td>366</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>368</td>
<td></td>
</tr>
<tr>
<td>A.32 Indication Expansion/New Dosage Strength</td>
<td>369</td>
<td></td>
</tr>
<tr>
<td>Zometa/Reclast® (Aclasta)</td>
<td>369</td>
<td></td>
</tr>
<tr>
<td>Learnings</td>
<td>370</td>
<td></td>
</tr>
</tbody>
</table>