

ANTIFUNGAL DRUGS: TECHNOLOGIES AND GLOBAL MARKETS



PHM029E
June 2014

Mary Anne Crandall
Project Analyst

ISBN: 1-56965-858-7

bcc | Research
Market Forecasting

BCC Research
49 Walnut Park, Building 2
Wellesley, MA 02481 USA
866-285-7215 (toll-free within the USA),
or (+1) 781-489-7301
www.bccresearch.com
information@bccresearch.com

TABLE OF CONTENTS

TOPIC	PAGE NO.
CHAPTER 1 INTRODUCTION	2
STUDY GOALS AND OBJECTIVES	2
REASONS FOR DOING THIS STUDY	2
INTENDED AUDIENCE	3
SCOPE OF REPORT	3
METHODOLOGY	4
INFORMATION SOURCES	4
ANALYST CREDENTIALS	4
RELATED BCC RESEARCH REPORTS	4
BCC RESEARCH WEBSITE	4
DISCLAIMER	5
CHAPTER 2 SUMMARY	7
<i>SUMMARY TABLE GLOBAL MARKET FORECAST FOR HUMAN ANTIFUNGAL THERAPEUTICS, BY GEOGRAPHIC REGION, THROUGH 2018 (\$ MILLIONS)</i>	7
<i>SUMMARY FIGURE GLOBAL MARKET FORECAST FOR HUMAN ANTIFUNGAL THERAPEUTICS, BY GEOGRAPHIC REGION, 2012-2018 (\$ MILLIONS)</i>	8
CHAPTER 3 OVERVIEW	10
HISTORY AND CURRENT STATE OF ANTIFUNGALS	10
TYPES OF PATHOGENIC FUNGI	11
DEFINITION OF THE INDUSTRY	11
CONCEPTS IN THE INDUSTRY	11
IMPORTANCE OF THE INDUSTRY	12
PRODUCT LIFE CYCLES	13
<i>TABLE 1 DRUG DEVELOPMENT LIFECYCLE FOLLOWING DISCOVERY OF NEW DRUG</i>	14
DEVELOPMENT OF ANTIFUNGALS	14
FDA-APPROVED ANTIFUNGALS	15
AZOLE ANTIFUNGALS	15
ECHINOCANDINS	16
POLYENES	16
ALLYLAMINES	16
MISCELLANEOUS ANTIFUNGALS	16
FUTURE DEVELOPMENTS	16
HUMAN CLINICAL DEVELOPMENT, 2011 TO 2013	17
NEW DRUG ACTIVITY	18
<i>TABLE 2 CLINICAL TRIALS OF ALL ANTIFUNGAL DRUG THERAPIES AND COMBINATIONS BY ALL DATE FIELDS, 2011-2013 (NUMBER)</i>	18
<i>TABLE 3 SELECTED GLOBAL CLINICAL TRIALS OF ALL ANTIFUNGAL DRUG THERAPIES THAT EITHER ARE COMPLETED OR ESTIMATED TO BE COMPLETED BETWEEN 2009 AND 2013 (NUMBER)</i>	19
ACTIVE OR COMPLETED STUDIES POSTED OR UPDATED, 2009 TO 2013	19
<i>TABLE 4 SELECTED ACTIVE OR COMPLETED STUDIES, 2009 TO 2014</i>	19
CHAPTER 4 INTRODUCTION TO INDUSTRY APPLICATIONS OF ANTIFUNGAL MEDICINAL THERAPEUTICS	23
SCOPE OF APPLICATIONS: HUMAN HEALTHCARE	23

TOPIC	PAGE NO.
HUMAN FUNGAL INFECTIONS	24
RISK FACTORS FOR DEVELOPING FUNGAL INFECTIONS	25
<i>TABLE 5 RISK FACTORS ASSOCIATED WITH HUMAN FUNGAL INFECTIONS</i>	26
FUNGAL SPECIES THAT CAUSE INFECTION IN HUMANS	27
Candidiasis	27
Some Basic Facts about Candida Infections	27
Cutaneous Candidiasis	30
Chronic Mucocutaneous Candidiasis	30
GI Tract Candidiasis	30
Respiratory Tract Candidiasis	30
Genitourinary Tract Candidiasis	31
Hepatosplenic Candidiasis	31
Systemic Candidiasis	31
Candidemia	31
Disseminated Candidiasis	32
Aspergillosis	33
Blastomycosis	34
Coccidioidomycosis	34
Cryptococcosis	36
Dermatophytosis	37
Histoplasmosis	38
Onychomycosis	39
Paracoccidioidomycosis	40
Pseudallescheriasis	40
Sporotrichosis	41
Zygomycosis	41
<i>TABLE 6 INCIDENCE OF COMMON FUNGAL DISEASES</i>	43
MORE RARE FUNGAL INFECTIONS AND DISORDERS	43
Literature Review	44
FUNGAL DRUG RESISTANCE	45
CURRENT DRUG RESISTANCE TOPICS: A GLOBAL VIEW	45
MDR SPECIES	46
Literature Review	48
<i>TABLE 7 COMMON REASONS FOR FUNGAL RESISTANCE</i>	49
STRATEGIES TO IMPROVE RESPONSE AND DECREASE MORTALITY	50
Literature Review	50
CHAPTER 5 HUMAN ANTIFUNGAL AGENTS	53
<i>TABLE 8 GLOBAL MARKET FORECAST FOR HUMAN ANTIFUNGAL CONSUMPTION BY PRODUCT TYPE, THROUGH 2018 (\$ MILLIONS)</i>	53
CLASSES OF ANTIFUNGALS	53
ECHINOCANDINS	53
Literature Review	54
AZOLES	54
Literature Review	55
POLYENES	55
Literature Review	55
OTHER	56

TOPIC	PAGE NO.
<i>TABLE 9 GLOBAL PRESCRIPTION ANTIFUNGAL PHARMACEUTICAL SALES - TRIAZOLES AND ECHINOCANDINS VERSUS OTHER ANTIFUNGALS, THROUGH 2018 (\$ MILLIONS)</i>	56
<i>TABLE 10 PHARMACEUTICAL ANTIFUNGALS BY CLASS/MECHANISM OF ACTION (%)</i>	57
<i>FIGURE 1 PERCENTAGE OF RECOGNIZED ANTIFUNGAL DRUGS (%)</i>	57
<i>TABLE 11 MAJOR ANTIFUNGAL AGENTS BY CLASS AND AVERAGE SALES PRICE PER DOSAGE, 2013</i>	58
<i>TABLE 12 FUNGAL INFECTION AND TRADITIONAL PHARMACEUTICAL REMEDY</i>	58
<i>TABLE 13 TYPES OF CANDIDAL INFECTION AND PHARMACEUTICAL TREATMENT</i>	60
SIDE EFFECTS	60
<i>TABLE 14 LIFE-THREATENING SIDE EFFECTS FROM ANTIFUNGAL PHARMACEUTICALS</i>	62
OTC ANTIFUNGAL PREPARATIONS	62
<i>TABLE 15 COMMON FUNGAL INFECTIONS AND OTC ROUTES OF ADMINISTRATION</i>	64
NATURAL ANTIFUNGAL REMEDIES	64
TYPES OF NATURAL ANTIFUNGAL REMEDIES	65
Herbal Remedies	66
Enzyme-Based Antifungal Agents	66
<i>TABLE 16 COMMON NATURAL ANTIFUNGALS</i>	68
SUMMARY OF SELECTED NATURAL ANTIFUNGALS	68
Aloe	68
Literature Review	69
Curcumin	70
Literature Review	70
Mint	70
Literature Review	71
Wild Marjoram	71
Literature Review	71
Radish	72
Literature Review	72
Parnafungins	73
Literature Review	73
Ginseng	74
Literature Review	74
Walnut	74
Literature Review	74
Pau d'arco	75
Literature Review	75
Garlic	75
Literature Review	75
Grapefruit Seed	76
Literature Review	76
Olive Leaf	76
Literature Review	76
Goldenseal	77
Literature Review	77
Oregano	77
Literature Review	77

TOPIC	PAGE NO.
Tea Tree	78
Literature Review	78
NATURAL REMEDIES IN EARLIER DEVELOPMENT	78
Literature Review	79
<i>TABLE 17 GLOBAL MARKET FORECAST FOR HUMAN OTC AND ALTERNATIVE ANTIFUNGAL CONSUMPTION BY PRODUCT TYPE, THROUGH 2018 (\$ MILLIONS)</i>	80
LABORATORY TESTING AND HISTOPATHOLOGY FOR FUNGAL INFECTIONS IN HUMANS	81
Specimen Examination	81
Cultures	81
Blood Serology	81
OTC/ALTERNATIVE HEALTHCARE APPROACHES TO TESTING AND DIAGNOSIS OF FUNGAL INFECTIONS	82
CAM Testing and Specialized Laboratories	82
Questionnaire for Symptoms	83
New Developments	83
CHAPTER 6 COMMON ENVIRONMENTAL FUNGI	85
MOLDS AND THE HUMAN ISSUES THEY PRODUCE	85
WHY ENVIRONMENTAL MOLD IS A UNIQUE PROBLEM	86
HEALTH RISKS DUE TO ENVIRONMENTAL FUNGI AND MOLD	87
<i>TABLE 18 COMMON HEALTH SYMPTOMS BASED ON ENVIRONMENTAL FUNGI AND MOLDS</i>	88
<i>TABLE 19 RISK FACTORS ASSOCIATION WITH ENVIRONMENTAL MOLD REACTIONS</i>	89
<i>TABLE 20 COMMON SOURCE LOCATIONS FOR ENVIRONMENTAL MOLDS</i>	89
ENVIRONMENTAL MOLDS	90
ALTERNARIA	90
Literature Review	90
ASPERGILLUS	91
Literature Review	91
CLADOSPORIUM	92
Literature Review	92
PENICILLIUM	93
Literature Review	93
EUROTIUM	94
Literature Review	94
RHIZOPUS	94
Literature Review	94
MUCOR	95
Literature Review	95
GEOTRICHUM	96
Literature Review	96
FUSARIUM	96
Literature Review	96
STACHYBOTRYS	97
Literature Review	97
WALLEMIA	97
Literature Review	98

TOPIC	PAGE NO.
TRICHOTHECIUM	98
Literature Review	98
SCOPULARIOPSIS BREVICAILIS	98
Literature Review	98
SCYTALIDIUM DIMIDIATUM	99
Literature Review	99
TRICHODERMA	100
Literature Review	100
PAECILOMYCES VARIOTII	101
Literature Review	101
CHAPTER 7 GOVERNMENT REGULATORY AGENCIES AND PROFESSIONAL ASSOCIATIONS	103
GOVERNMENT REGULATIONS	103
FDA	103
<i>TABLE 21 SELECTED ANTIFUNGAL WARNING LETTERS FOR THE HUMAN SEGMENT FROM THE FDA TO MANUFACTURERS, 1997-2014</i>	104
EPA	111
USDA	112
FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS	112
PROFESSIONAL ASSOCIATIONS	113
MEDICAL AND VETERINARY ASSOCIATIONS	113
AGRICULTURAL ASSOCIATIONS	113
OTHER ENVIRONMENTAL ASSOCIATIONS	113
CHAPTER 8 ANTIFUNGAL COMPANIES	115
HUMAN HEALTHCARE	115
MANUFACTURERS OF PRESCRIPTION PHARMACEUTICALS	115
<i>TABLE 22 MAJOR GLOBAL MANUFACTURERS OF ANTIFUNGAL PHARMACEUTICALS FOR HUMAN CONSUMPTION</i>	115
<i>FIGURE 2 GLOBAL ANTIFUNGAL PHARMACEUTICAL MANUFACTURERS BY COUNTRY (%)</i>	116
MAJOR PHARMACEUTICAL MANUFACTURER PROFILES	116
<i>TABLE 23 COMPETITIVE MARKET SHARE BY PERCENT, 2013 (%)</i>	117
<i>FIGURE 3 COMPETITIVE MARKET SHARE BY PERCENT, 2013 (%)</i>	117
Astellas Pharma Inc.	117
Bayer HealthCare	118
Enzon Pharmaceuticals	118
Galderma Pharma SA/Galderma SA	119
Gilead Sciences Inc.	119
Novartis International AG	119
Pfizer Inc.	120
Taro Pharmaceutical Industries, Ltd.	120
Taro USA Inc.	120
Teva Pharmaceutical Industries, Ltd.	120
Valeant Pharmaceuticals	121
OTC ANTIFUNGAL MANUFACTURERS	121
PHARMACEUTICAL OTC MARKET	122

TOPIC	PAGE NO.
<i>TABLE 24 MAJOR HUMAN OTC ANTIFUNGAL MANUFACTURERS AND PRODUCTS</i>	122
MAJOR PHARMACEUTICAL-BASED OTC MANUFACTURER PROFILES	122
Alva-Amco Pharmacal	122
Blaine Labs	123
Dartmouth Pharmaceuticals	123
Kramer Consumer Healthcare	123
Novartis International AG	124
McNeil Consumer Healthcare	124
PEDiNOL Pharmacal, Inc.	124
Perrigo Company plc	125
Stiefel Laboratories, Inc	125
Tarmac Products	126
ALTERNATIVE OTC MANUFACTURERS	126
<i>TABLE 25 COMMONLY AVAILABLE ALTERNATIVE ANTIFUNGALS</i>	126
MAJOR ALTERNATIVE OTC MANUFACTURER PROFILES	127
Crystal Star Herbal Nutrition	127
Enzymedica	127
Forest Herbs Research Ltd.	127
Garden of Life	128
King Bio	128
Life Extension Nutrition Center	128
Michael's Naturopathic Programs	129
Nature's Plus	129
NOW Foods	129
Nutrition Now	130
PROSymbiotics	130
Pure Essence Laboratories	130
Rainbow Light	131
Renew Life	131
Solaray	131
Vitanica	132
CHAPTER 9 ANTIFUNGAL INDUSTRY	134
ANTIFUNGAL MARKET TRENDS: HUMAN HEALTHCARE	134
ACCELERATING ANTIFUNGAL DRUG DEVELOPMENT	134
<i>TABLE 26 NEW PRESCRIPTION ANTIFUNGALS, 2005 TO MARCH 2014</i>	135
INCREASED TYPES OF TESTING	136
Need to Increase Use and Acceptance of Newer Drugs	136
EXPERIMENTAL RESEARCH - CLINICAL TRIALS PERFORMED AND SELECTED PRECLINICAL AND IN VIVO STUDIES	137
A GENERAL OVERVIEW OF NONPHARMACEUTICAL ANTIFUNGAL TECHNOLOGIES	138
Laser and Photodynamic Therapy	138
Studies	138
Literature Review	138
mAbs	139
Diagnostics and Assays	139
Literature Review	140

TOPIC	PAGE NO.
Computer Modeling Technology	140
Literature Review	140
R&D SECTION: AN OVERVIEW OF PRODUCTS IN DEVELOPMENT	141
<i>TABLE 27 ANTIFUNGALS IN DEVELOPMENT</i>	142
TRENDS IN CLASS USED AND ADMINISTRATION METHOD	142
<i>TABLE 28 PHARMACEUTICAL ANTIFUNGALS BY ROUTE OF ADMINISTRATION 2013 (%)</i>	143
<i>FIGURE 4 PHARMACEUTICAL ANTIFUNGALS BY ROUTE OF ADMINISTRATION, 2013 (%)</i>	143
<i>TABLE 29 GLOBAL MARKET FORECAST FOR ANTIFUNGAL PRODUCTS BY ROUTE OF ADMINISTRATION, THROUGH 2018 (\$ MILLIONS)</i>	144
UTILIZATION OF OTC AND NATURAL/ALTERNATIVE ANTIFUNGAL AGENTS	144
Shifting the Market from Prescription to OTC	144
Market Demand for OTC Products	144
CHAPTER 10 PATENT ANALYSIS	147
PURPOSE OF A PATENT ANALYSIS	147
DUE CARE IN REVIEWING THE PATENT ANALYSIS	147
NEW ANTIFUNGAL PATENTS ISSUED	148
<i>TABLE 30 U.S. ANTIFUNGAL PATENT TRENDS, 1990-2013</i>	148
<i>TABLE 31 SELECTED NEW U.S. ANTIFUNGAL PATENTS ISSUED 2007-2013</i>	149
<i>TABLE 32 ASSIGNEES OF TWO OR MORE U.S. PATENTS FOR ANTIFUNGAL PRODUCTS, 2007-2013</i>	151
<i>TABLE 33 U.S. PATENT TRENDS BY COUNTRY, 2007-2013 (NO. OF PATENTS/%)</i>	152
<i>FIGURE 5 U.S. PATENT TRENDS BY COUNTRY, 2007-2013 (%)</i>	152
TRENDS IN PATENT APPLICATIONS	153
<i>TABLE 34 U.S. PATENT APPLICATIONS BY ANTIFUNGAL MECHANISM OF ACTION, 2007-2013 (NO./%)</i>	153
<i>FIGURE 6 U.S. PATENT APPLICATIONS BY ANTIFUNGAL MECHANISM OF ACTION, 2007 THROUGH 2013 (%)</i>	153
<i>TABLE 35 NEW U.S. PATENT APPLICATIONS, 2007-2013</i>	154
<i>TABLE 36 RECENT TRENDS IN PATENT APPLICATIONS FOR ANTIFUNGALS BY MECHANISM OF ACTION, 2007-2013</i>	160
<i>TABLE 37 U.S. PATENT APPLICATION TRENDS BY COUNTRY, 2007-2013 (NO. OF PATENTS/%)</i>	160
<i>FIGURE 7 U.S. ANTIFUNGAL PATENT APPLICATIONS BY COUNTRY 2007-2013 (%)</i>	160
PATENT EXPIRATIONS	161
<i>TABLE 38 PATENT EXPIRATIONS 2006-2018</i>	162
CHAPTER 11 APPENDIX	164
<i>TABLE 39 PHARMACEUTICAL COMPANIES</i>	164

LIST OF TABLES

TABLE HEADING	PAGE NO.
SUMMARY TABLE GLOBAL MARKET FORECAST FOR HUMAN ANTIFUNGAL THERAPEUTICS, BY GEOGRAPHIC REGION, THROUGH 2018 (\$ MILLIONS)	7
TABLE 1 DRUG DEVELOPMENT LIFECYCLE FOLLOWING DISCOVERY OF NEW DRUG	14
TABLE 2 CLINICAL TRIALS OF ALL ANTIFUNGAL DRUG THERAPIES AND COMBINATIONS BY ALL DATE FIELDS, 2011-2013 (NUMBER)	18
TABLE 3 SELECTED GLOBAL CLINICAL TRIALS OF ALL ANTIFUNGAL DRUG THERAPIES THAT EITHER ARE COMPLETED OR ESTIMATED TO BE COMPLETED BETWEEN 2009 AND 2013 (NUMBER)	19
TABLE 4 SELECTED ACTIVE OR COMPLETED STUDIES, 2009 TO 2014	19
TABLE 5 RISK FACTORS ASSOCIATED WITH HUMAN FUNGAL INFECTIONS	26
TABLE 6 INCIDENCE OF COMMON FUNGAL DISEASES	43
TABLE 7 COMMON REASONS FOR FUNGAL RESISTANCE	49
TABLE 8 GLOBAL MARKET FORECAST FOR HUMAN ANTIFUNGAL CONSUMPTION BY PRODUCT TYPE, THROUGH 2018 (\$ MILLIONS)	53
TABLE 9 GLOBAL PRESCRIPTION ANTIFUNGAL PHARMACEUTICAL SALES - TRIAZOLES AND ECHINOCANDINS VERSUS OTHER ANTIFUNGALS, THROUGH 2018 (\$ MILLIONS)	56
TABLE 10 PHARMACEUTICAL ANTIFUNGALS BY CLASS/MECHANISM OF ACTION (%)	57
TABLE 11 MAJOR ANTIFUNGAL AGENTS BY CLASS AND AVERAGE SALES PRICE PER DOSAGE, 2013	58
TABLE 12 FUNGAL INFECTION AND TRADITIONAL PHARMACEUTICAL REMEDY	58
TABLE 13 TYPES OF CANDIDAL INFECTION AND PHARMACEUTICAL TREATMENT	60
TABLE 14 LIFE-THREATENING SIDE EFFECTS FROM ANTIFUNGAL PHARMACEUTICALS	62
TABLE 15 COMMON FUNGAL INFECTIONS AND OTC ROUTES OF ADMINISTRATION	64
TABLE 16 COMMON NATURAL ANTIFUNGALS	68
TABLE 17 GLOBAL MARKET FORECAST FOR HUMAN OTC AND ALTERNATIVE ANTIFUNGAL CONSUMPTION BY PRODUCT TYPE, THROUGH 2018 (\$ MILLIONS)	80
TABLE 18 COMMON HEALTH SYMPTOMS BASED ON ENVIRONMENTAL FUNGI AND MOLDS	88
TABLE 19 RISK FACTORS ASSOCIATION WITH ENVIRONMENTAL MOLD REACTIONS	89
TABLE 20 COMMON SOURCE LOCATIONS FOR ENVIRONMENTAL MOLDS	89
TABLE 21 SELECTED ANTIFUNGAL WARNING LETTERS FOR THE HUMAN SEGMENT FROM THE FDA TO MANUFACTURERS, 1997-2014	104
TABLE 22 MAJOR GLOBAL MANUFACTURERS OF ANTIFUNGAL PHARMACEUTICALS FOR HUMAN CONSUMPTION	115
TABLE 23 COMPETITIVE MARKET SHARE BY PERCENT, 2013 (%)	117
TABLE 24 MAJOR HUMAN OTC ANTIFUNGAL MANUFACTURERS AND PRODUCTS	122
TABLE 25 COMMONLY AVAILABLE ALTERNATIVE ANTIFUNGALS	126
TABLE 26 NEW PRESCRIPTION ANTIFUNGALS, 2005 TO MARCH 2014	135
TABLE 27 ANTIFUNGALS IN DEVELOPMENT	142
TABLE 28 PHARMACEUTICAL ANTIFUNGALS BY ROUTE OF ADMINISTRATION 2013 (%)	143
TABLE 29 GLOBAL MARKET FORECAST FOR ANTIFUNGAL PRODUCTS BY ROUTE OF ADMINISTRATION, THROUGH 2018 (\$ MILLIONS)	144
TABLE 30 U.S. ANTIFUNGAL PATENT TRENDS, 1990-2013	148
TABLE 31 SELECTED NEW U.S. ANTIFUNGAL PATENTS ISSUED 2007-2013	149
TABLE 32 ASSIGNEES OF TWO OR MORE U.S. PATENTS FOR ANTIFUNGAL PRODUCTS, 2007-2013	151
TABLE 33 U.S. PATENT TRENDS BY COUNTRY, 2007-2013 (NO. OF PATENTS/%)	152

TABLE HEADING	PAGE NO.
TABLE 34 U.S. PATENT APPLICATIONS BY ANTIFUNGAL MECHANISM OF ACTION, 2007-2013 (NO./%)	153
TABLE 35 NEW U.S. PATENT APPLICATIONS, 2007-2013	154
TABLE 36 RECENT TRENDS IN PATENT APPLICATIONS FOR ANTIFUNGALS BY MECHANISM OF ACTION, 2007-2013	160
TABLE 37 U.S. PATENT APPLICATION TRENDS BY COUNTRY, 2007-2013 (NO. OF PATENTS/%)	160
TABLE 38 PATENT EXPIRATIONS 2006-2018	162
TABLE 39 PHARMACEUTICAL COMPANIES	164

LIST OF FIGURES

FIGURE TITLE	PAGE NO.
SUMMARY FIGURE GLOBAL MARKET FORECAST FOR HUMAN ANTIFUNGAL THERAPEUTICS, BY GEOGRAPHIC REGION, 2012-2018 (\$ MILLIONS)	8
FIGURE 1 PERCENTAGE OF RECOGNIZED ANTIFUNGAL DRUGS (%)	57
FIGURE 2 GLOBAL ANTIFUNGAL PHARMACEUTICAL MANUFACTURERS BY COUNTRY (%)	116
FIGURE 3 COMPETITIVE MARKET SHARE BY PERCENT, 2013 (%)	117
FIGURE 4 PHARMACEUTICAL ANTIFUNGALS BY ROUTE OF ADMINISTRATION, 2013 (%)	143
FIGURE 5 U.S. PATENT TRENDS BY COUNTRY, 2007-2013 (%)	152
FIGURE 6 U.S. PATENT APPLICATIONS BY ANTIFUNGAL MECHANISM OF ACTION, 2007 THROUGH 2013 (%)	153
FIGURE 7 U.S. ANTIFUNGAL PATENT APPLICATIONS BY COUNTRY 2007-2013 (%)	160