Contents

Foreword, ix
Acknowledgement, xi
Author’s note on the cover design, xiii
Introduction, xv

1 What is off-label medication, and how prevalent is it?, 1
   What is ‘off-label’ medicine?, 2
   Scope of the issue, 8

2 Where it all went right: new uses for existing drugs supported by good evidence, 19
   Examples where products have been through regulatory approval for a secondary use, 19
   Finasteride: pseudohermaphroditism and hair growth, 19
   Sildenafil: re-tasking the blue pill for a life-threatening illness, 21
   Doxycycline: from killing bugs to protecting gums, 22
   Raloxifene: from cancer to bone disease and back again, 23
   Galantamine: using snowdrops to improve memory, 24
   Cyclosporine: preventing immune attack on organs and skin, 25
   Dimethyl fumarate: a remarkable drug for multiple sclerosis, 26
   Botox: a drug to kill or cure you, 27
   Examples where evidence is uncertain and not to regulatory standards, 28
   Tricyclic antidepressants: for curing more than emotional pain, 28
   Aspirin for cancer, 30
   Retrospective data: looking back to create future therapies, 30

3 Shared decision making and consent, 33
   Viewpoint of the patient, 34
   Viewpoint of the prescriber, 37
   Professional guidelines, 38
   Patient awareness, 41
   Practitioner attitudes, 41
   Diagnosis, 44

4 Gaming the system: the role of the pharmaceutical industry, 47
   Normal drug development and drug repurposing development, 48
   Gaming the system, 53
   Orphan use, 56
   Pharmaceutical marketing, 61
   Expanding uses for non-pharmaceuticals, 64
   DTC advertising, 64
   Patents and genericisation, 65
   Conclusion, 68

5 Do no harm: Safety and efficacy, 71
   Relative safety, 73
Different therapeutic uses, 73
Chronic versus acute dosing, 78
Different dose, 81
Differences between children and adults, 82
Other patient populations, 86
Fatal ADRs, 87
Quality of evidence, 88
Strong evidence, 89
Poor evidence, 91
Doctors do not know evidence, 94
Proximity of off-label to on-label, 96
Debunking medical myths, 101

6 Liability, injustice and reimbursement: who should pay?, 105
A prescriber’s ethical and professional duties, 105
Medical professional participation in off-label promotion, 105
A prescriber’s legal position, 106
Consent, 106
Liability, 111
Reimbursement, 113
Compendia, 115
NICE, 117
Compassionate access, 120
Cost, as a driver for off-label medicine, 121

7 The role of regulation in off-label medicine, 125
Regulators do not regulate medical practice, 126
Off-label marketing, 128
Off-label fines, 130
Whistle-blowers, 134
European situation, 134
Tip of the iceberg, 136
Free speech, 138

8 Justifying unapproved medicine, 143
Constraints on making changes, 144
Moves to enhance off-label medicine, 145
Diagnosis shifting, 146
A partial solution: clinical trial transparency, 147
A solution based on increased regulatory supervision, 152
My solutions, 153
Professional standards, 153
Reimbursement and pricing, 156
Outcomes, 159
Conclusion, 173

References, 175
Index, 191