

## INDEX

Note: Page numbers in *italics> indicate figures.  
Page numbers followed by a “t” indicate tables.  
Clinical trials are listed by their acronyms.*

- A1C. See *Glycosylated hemoglobin (A1C)*.
- Academy of Nutrition and Dietetics, 477
- Acarbose (Precose), 84t, 199-200  
in combination therapy, 200, 210  
dose, 84t, 200, 201t  
for metabolic syndrome, 1  
prescribing information, 200, 201t  
side effects, 200  
in Stop-NIDDM, 462t, 465
- ACCORD trial, 77-80, 79
- ACE inhibitors, 29, 408-411, 412  
benefits of, 407, 408-410, 410t, 411  
cardioprotective effect, 408-410  
renal benefits, 408, 410, 435  
cardioprotective effect of, 408, 435  
cautions for, 411, 435  
complications of, 409t, 410  
for metabolic syndrome, 1  
potassium monitoring for, 410
- Acetohexamide (Dymelor), 87t, 203
- Acidosis. See *Diabetic ketoacidosis (DKA)*.
- Acquired factors in type 2 diabetes, 25-26
- ACT-NOW trial, 462t, 466-467, 467
- Actoplus Met (pioglitazone/metformin), 88t, 184, 186t-187t. See also *Metformin*; *Pioglitazone*.  
prescribing considerations, 190-191
- Actos. See *Pioglitazone*.
- Adlyxin. See *Lixisenatide*.
- Adolescents, type 2 diabetes in, 38
- ADVANCE trial, 77-80
- Afrezza (inhaled insulin), 259-263  
administration and dosage, 259-260, 260  
efficacy, 260, 262t  
pharmacokinetics, 260, 261  
pulmonary function and, 263  
safety, 262-263  
time course of action, 232t, 235, 259
- African Americans, 15, 17, 18. See also *Race/ethnicity*.
- Age  
aging process, and T2D, 25-26, 27  
incidence of diabetes and, 15, 16, 18, 20, 21, 25-26, 35  
of onset  
maturity-onset diabetes of the young (MODY), 38  
type 1 diabetes, 34  
type 2 diabetes, 35  
prevalence of diabetes and, 16, 16  
as risk factor for cardiovascular disease, 49  
as risk factor for diabetes, 37, 42  
Alaskan natives, 15, 17, 18
- Albiglutide (Tanzeum), 313-323  
action mechanism, 313  
advantages of, 313  
adverse events, 320, 322  
in algorithm for treatment, 358  
in combination therapy, 313, 319-321  
contraindications, 322  
dosage and administration, 297t, 322-323  
efficacy, 313-319, 314t-318t, 321  
FDA approval of, 287  
half-life, 313  
indications for, 313  
monotherapy, 319, 320, 321  
safety and tolerability, 322  
weight effects of, 319-320
- Albuminuria, 49, 405, 431
- Alcohol use/intake, 60t, 64-65, 419  
diabetic ketoacidosis and, 386t  
sugar alcohols, 63
- Algorithms  
for insulin therapy, 239  
for treatment of T2D, 355-360, 358-359
- Alirocumab, 421-422
- ALLHAT, 412, 470t
- Alogliptin (Nesina), 84t, 127-141  
adverse events, 139  
cardiovascular outcomes, 138  
combination formulations  
alogliptin/metformin (Kazano), 85t, 140  
alogliptin/pioglitazone (Oseni), 85t, 140-141  
combination therapy  
with glyburide, 135t, 137  
with insulin, 135t, 137  
with metformin, 129-131, 132t, 134t, 136-137  
with pioglitazone, 131, 133t, 134t-135t, 136-137  
with SFU, 136-137  
dosage, 84t, 139-140  
efficacy, 129-137  
hyperglycemia and, 139  
hypoglycemia and, 139  
pharmacokinetics, 127-129  
prescribing, 139-140  
trials and studies, 129-131, 132t-133t
- $\alpha$ -Blockers, 409t, 410t, 411, 436
- $\alpha$ -Cell hormone. See *Glucagon*.
- Alpha-glucosidase inhibitors, 29, 84t, 199-202. See also *Acarbose*; *Miglitol*.  
action mechanism, 199  
in algorithm for treatment, 358  
combination therapy, 200  
dosing, 84t, 200, 201t, 202  
side effects, 200, 202
- ALTTITUDE study, 411
- Amaryl. See *Glimepiride*.
- American Association of Clinical Endocrinologists (AAACE), 357
- American Association of Diabetes Educators (AADE), 477

- American Association of Kidney Patients (AAKP), 478
- American Diabetes Association (ADA), 478-479
- blood pressure goals, 406
  - dyslipidemia recommendations, 418
  - hypoglycemia definition, 396
  - targets/goals for glycemic control, 357, 405-406, 418
- American Heart Association, 479
- American Indians, 15, 17, 31
- Indian DPP trial, 462t
  - Indian Health Services (IHS), 480
  - prevalence of diabetes in, 15, 17, 18
- Amlodipine, 412
- Amylin, 283, 284, 343. See also *Pramlintide*.
- actions of, 343
  - cosecretion with insulin, 343, 344
  - deficiency in diabetes, 343, 344
  - gastric emptying and, 343
  - GLP-1 and, 283
- Amylin analogue (pramlintide), 343-350. See also *Pramlintide*.
- Angiotensin-converting enzyme inhibitors. See *ACE inhibitors*.
- Angiotensin II receptor blockers. See *ARBs*.
- Ankle-brachial index (ABI), 445
- Antibodies
- to GAD, 34, 228
  - to islet cells (ICA), 228
- Antidepressants, 438
- Antihypertensive drugs, 407-412, 409t, 435-436. See also *Hypertension; specific agents*.
- choice of, 412
  - complications of, 409t
  - new-onset diabetes and, 411, 470
  - potential benefits of, 407-412, 410t
- Antioxidant supplements, 64
- Apidra. See *Glulisine*.
- Apolipoprotein A1, 414t
- Apolipoprotein B, 414t, 416-417, 417t
- ARBs (angiotensin II receptor blockers), 408, 410-411, 412
- benefits of, 408, 410-411, 410t, 435
  - cautions for, 411, 435
  - complications of, 409t
  - for metabolic syndrome, 51
- ARIC study, 411
- Asian/Asian-American patients, 15, 17, 41, 228. See also *Race/ethnicity*.
- Aspart (Novolog), 228, 229, 249, 257-258
- time course of action, 230, 232t, 235
- Aspirin therapy, 77, 355
- Assessment of treatment regimen, 361-382
- advances in glucose monitoring, 373-379
  - continuous glucose monitoring systems, 379-380
  - fructosamine and other glycated proteins, 364-365, 365, 371
  - glycated hemoglobin measurement, 363-364
  - metabolic goals, 362t
  - plasma glucose concentrations, 361-363
  - self-monitoring of blood glucose, 366-373. See also *Self-monitoring of blood glucose (SMBG)*.
- Associations and resources on diabetes, 477-484
- Asymptomatic diabetes, 16-18, 28, 41
- Atenolol, 411
- Atherosclerosis, 71
- Atherosclerotic Vascular Disease (ASVD), 406, 422t
- Autoantibodies, 31-32, 34
- AUTONOMY study, 245-246
- Avanafil (Stendra), 442, 443t
- Avandamet (rosiglitazone/metformin), 88t
- Avandaryl (rosiglitazone/glimepiride), 88t
- Avandia. See *Rosiglitazone*.
- B-type natriuretic peptide (BNP), 193
- Basaglar U-100 (insulin glargine follow-on biologic), 269
- Belviq (lorcaserin), 451-453
- $\beta$ -Blockers, 409t, 410t, 411, 412
- $\beta$ -Cell
- exhaustion, 28, 205, 227
  - failure, 28, 81
  - function
    - compensation for insulin resistance, 25-26
    - decreased, in type 2 diabetes, 25, 26, 27-28
    - GLP-1 and, 293, 337
    - SFUs and, 205
  - hormones. See *Amylin; Insulin*.
- Bethanechol, 440
- Bicarbonate therapy, 388, 392, 396
- Biguanide. See *Metformin*.
- Bile acid sequestrant (colesevelam, Welchol), 84t, 217-221, 421t
- action mechanisms, 217
  - adverse events, 219
  - dosage, 84t
  - efficacy, 217-219, 220-221
  - in treatment of dyslipidemia, 217, 421t
- Biosimilar products, 269
- Blood glucose monitoring. See *Glucose monitoring*.
- Blood pressure. See also *Hypertension*.
- hypertension, 406-412
  - hypotension, 407
  - orthostatic, 411, 440
  - and renal disease, 432-433
  - target/goal levels, 362t, 406-407
- Bloodletting devices, 373-379
- Blurred vision, 41, 400
- BMI (body mass index), 56t
- Body fat, distribution of, 27, 37. See also *Obesity*.
- Body mass index (BMI), 56t
- Body weight. See *Weight*.
- Bromocriptine mesylate (Cycloset), 84t, 223-226
- action mechanism, 223
  - adverse events, 224-225
  - in algorithm for treatment, 358
  - contraindications, 225
  - dosage, 84t, 225
  - efficacy, 223-224
  - prescribing information, 225

- Bydureon (extended-release exenatide), 295-298, 298t. See also *Exenatide*.  
Byetta. See *Exenatide*.
- C-peptide levels, 240
- Calcium channel blockers (CCBs), 409t, 410t, 411-412, 436
- Caloric intake, 55, 57-58. See also *Diet; Nutrition; Weight*.
- Canadian Diabetes Association, 243t
- Canagliflozin (Invokana), 86t, 147-157  
action mechanism, 147  
adverse events, 151t, 152-157, 156t  
blood pressure, effect on, 152  
body weight, effect on, 152, 155  
combination agent with metformin (Invokamet, Invokamet XR), 86t  
in combination therapy  
with insulin, 149t  
with metformin, 147, 148t-149t  
with metformin/SFU, 149t  
dosage, 86t, 157  
efficacy, 147-152  
phase 3 studies, 148t-150t, 153, 154, 155  
prescribing information, 157  
safety, 151t, 152-157, 156t
- CAPPP (Captopril Prevention Project), 470t
- Capsaicin cream, 438
- Captopril, 470t
- Carbohydrates, 59-62, 60t  
carrying a source of (for hypoglycemia treatment), 399
- Cardiovascular autonomic neuropathy (CAN), 440
- Cardiovascular outcomes  
with alogliptin, 138  
with empagliflozin, 175, 176-178, 423  
with linagliptin, 123  
with liraglutide (LEADER trial), 309-313, 312, 423  
morbidity and mortality, 45-48, 181, 405, 406, 408  
with saxagliptin, 116  
with sitagliptin, 105-106
- Cardiovascular risk, 45-49, 71, 181, 405-406  
ADA listing of, 48-49  
antihypertensive agents and, 407-412  
assessment of, 361  
bromocriptine mesylate and, 224-225  
diabetes as CV disease equivalent, 45  
dyslipidemia and, 413, 414t  
hypertension and, 48, 406  
pioglitazone and, 193-194, 194t  
reduced  
in ACCORD and ADVANCE trials, 77-80, 79  
with antihypertensive agents, 407-412, 410t, 435  
with glycemic control, 75-80, 405-406  
with multifactorial treatment, 405-406  
with pioglitazone, 185-188, 188  
in Steno-2 Trial, 77, 78  
with thiazolidinediones (TZDs), 181  
in UKPDS, 75-77, 75t  
rosiglitazone and, 194-196  
sulfonylureas and, 205
- CCBs. See *Calcium channel blockers*.
- CDC (Centers for Disease Control), 479-480
- Cellulitis, 402t
- Centers for Disease Control. See *CDC*.
- Central obesity. See *Obesity, central*.
- Cerebrovascular accident, 386t, 395
- Cerebrovascular disease, 405, 406
- Cerebrovascular edema, 393
- CHF (congestive heart failure), TZDs and, 193-194, 194t
- Children  
screening for prediabetes, 28  
type 2 diabetes in, 35, 38
- Chlorpropamide (Diabinese), 87t, 203, 204
- Chlorthalidone, 412
- Cholesterol levels, 413, 414t. See also *Dyslipidemia; HDL; LDL*.  
cholesterol absorption inhibitors, 421t  
lipid-lowering drugs, 417, 420-423, 421t  
measurements, 414-418  
non-HDL-C, 417-418  
target/goal levels, 414, 417t  
total cholesterol, 414-415, 417t
- Cialis (tadalafil), 442, 443t
- Classification of diabetes mellitus, 31-39, 32t-33t  
gestational diabetes (GDM), 32t, 35-36  
impaired fasting glucose (IFG), 37t  
impaired glucose tolerance (IGT), 33t  
latent autoimmune diabetes in adults (LADA), 32t, 34  
other types, 32t-33t, 37  
problems with, 38  
type 1 diabetes (T1D), 31-34, 32t  
type 2 diabetes (T2D), 32t, 34-35
- Cognitive impairment, 383, 395
- Colesevelam (Welchol), 84t, 217-221  
action mechanisms, 217  
adverse events, 219  
in algorithm for treatment, 358  
contraindications, 219-221  
dosage, 84t  
dyslipidemia treatment with, 217, 417  
efficacy (glycemic control), 217-219, 220-221  
prescribing information, 219
- Complications of diabetes, 383-448. See also *specific conditions*.  
acute, 383-404  
diabetic ketoacidosis (DKA), 383-393  
hyperosmolar hyperglycemic syndrome (HHS), 394-396  
hypoglycemia, 396-400  
infection, 400, 402t-403t  
quality of life, 383, 400  
assessing evidence for, 361  
delay/prevention with good glycemic control, 74-75, 75t, 355, 356, 425-426  
early detection and treatment, reduction with, 29, 51, 425-426  
hyperglycemia and, 74  
long-term, 405-428  
diabetic nephropathy, 431-436  
diabetic neuropathy, 436-444, 437t

- Complications of diabetes, long-term (*continued*)  
 diabetic retinopathy, 425-430  
 dyslipidemia, 413-423  
 erectile dysfunction, 441-444, 443t  
 exercise and, 68  
 foot disorders, 444-445  
 hypertension, 406-412  
 macrovascular disease, 405-424  
 microvascular complications, 425-448  
 reducing risk with multifactorial treatment, 404-405  
 metabolic complications, 383-400  
 postprandial hyperglycemia and, 73-74  
 Congestive heart failure (CHF). See *CHF*  
 CONQUER trial, 468-469, 470t  
 Continuous glucose monitoring systems, 379-380  
 Contrave (naltrexone/bupropion), 453-455  
 Coronary events, antihypertensive agents and, 410t, 412  
 Corticosteroids, for diabetic retinopathy, 430  
 Cushing's syndrome, diabetes secondary to, 32t  
 Cutaneous infections, 402t  
 Cycloset. See *Bromocriptine mesylate*.
- Da Qing IGT and Diabetes Study, 461-462, 462t  
 Dapagliflozin (Farxiga), 86t, 158-167  
 adverse reactions, 159-167, 166t  
 body weight, effect on, 158, 165  
 combination agent with metformin (Xigduo XR), 86t  
 combination therapy, 158-159, 160t-162t, 163-165  
 dosage and prescribing information, 86t, 167  
 efficacy, 158-159, 160t-162t, 163, 164  
 safety, 159-167, 166t  
 DASH diet, 59, 407, 419-420  
 DCCT (Diabetes Control and Complications Trial), 367  
 Degludec + aspart injection (Ryzodeg), 229, 233t, 244, 275, 276-278  
 in algorithm for treatment, 358  
 time course of action, 233t  
 Degludec + liraglutide (Xultophy 100/3.6), 338-340  
 Degludec U-100 and U-200 (Tresiba), 229, 245, 271-275  
 efficacy, 273-274  
 safety, 274-275  
 starting or switching to, 274  
 time course of action, 233t  
 Dehydration, 384, 385  
 Detemir (Levemir), 229, 245, 266  
 time course of action, 233t, 235  
 Dextrose, 393  
 DiaBeta (glyburide). See *Glyburide*.  
 Diabetes mellitus  
 cardiovascular disease risk and, 45-49  
 characteristics of, 23-25, 24, 27-28  
 classification of, 31-39, 32t-33t  
 complications of, 383-448  
 diagnosis of, 41-52, 43t  
 heterogeneous pathophysiology of, 23-25  
 incidence of, 15, 16-18, 16, 20, 21  
 Diabetes mellitus (*continued*)  
 insulin-dependent. See *Type 1 diabetes (T1D)*.  
 new-onset, antihypertensive agents and, 411, 470  
 non-insulin-dependent. See *Type 2 diabetes (T2D)*.  
 prevalence of, 15-18, 16, 17  
 prevention of, 29, 461-475  
 resources on, 477-484  
 secondary to other conditions, 32t-33t  
 subclasses of, 31-36  
 symptoms of, 27, 41  
 Diabetes Prevention Program (DPP), 91, 462t, 463-464  
 Diabetes prevention trials. See *Primary prevention trials*.  
 Diabetes Warranty Program, 45, 46-47  
 Diabetic dyslipidemia. See *Dyslipidemia*.  
 Diabetic ketoacidosis (DKA), 383-393  
 criteria for, 384t, 389t  
 differential diagnosis, 388, 390t  
 laboratory evaluation, 387-388, 389t  
 mortality from, 393  
 pathophysiology of, 385  
 precipitating factors, 384-385, 386t  
 prevention of, 393  
 signs and symptoms, 384, 385-387  
 treatment, 388-393  
 bicarbonate therapy, 388, 392  
 complications of, 393  
 fluid therapy, 388, 390  
 insulin infusion, 388, 391, 392-393  
 phosphate replacement, 388, 392  
 potassium replacement, 388, 391-392  
 Diabetic nephropathy, 431-436, 432-433, 434t  
 classification/staging of, 432, 433t  
 evaluation/screening for, 432-433, 434t  
 factors contributing to, 431-432  
 treatment, 433-435  
 antihypertensive therapy, 435-436  
 empagliflozin, 433-435  
 glycemic control, improved, 435  
 protein restriction, 436  
 SGLT2 inhibitors, 435  
 Diabetic neuropathy, 436-444  
 glycemic control and, 436  
 painful neuropathies, 437-438  
 types of, 437t  
 autonomic, 437t  
 cardiovascular autonomic neuropathy (CAN), 440  
 diabetic amyotrophy, 438-439  
 diabetic peripheral neuropathy (DPN), 437-438, 437t  
 gastroparesis, 439-440  
 mononeuropathy, 438  
 neurogenic bladder, 440  
 Diabetic retinopathy, 18, 425-430  
 categories of, 426-427  
 nonproliferative, 426, 427  
 preproliferative, 426-427, 428  
 proliferative, 427

- Diabetic retinopathy (*continued*)  
 early diagnosis, value of, 425-426  
 evaluation and referral, 428, 429t  
 exercise and, 68  
 eye exams, 425-426, 428, 429t  
 patient education on, 426  
 treatment, 429-430  
   photocoagulation surgery, 429-430  
   VEGF inhibitors, 430  
 trials on, 429-430
- Diabinese. See *Chlorpropamide*.
- Diagnosis of diabetes, 41-52, 43t  
 asymptomatic presentation, 41  
 cardiovascular risk assessment and, 45-49  
 criteria for, 42, 43t, 358  
   fasting blood glucose, 16, 42, 43t, 358  
   plasma glucose concentration, 42, 43t, 44  
   for prediabetes, 36-37, 37t, 43t  
   signs and symptoms, 27, 41  
 early, importance of, 29, 41, 81, 425-426  
 glucose testing/levels, 42-44, 43t  
 medical evaluation, 45, 46-47  
 problems with, 38
- Diagnosis of metabolic syndrome, 49-51, 50t
- Diet, 53-66, 355, 357. See also *Nutrition; Obesity; Weight*.  
 adjustments, glucose monitoring for, 54, 62, 370-371  
 body weight considerations, 55-57, 56t  
 caloric intake, 55, 57-58  
 DASH diet, 59, 407, 419-420  
 diabetes prevention and, 462t  
 dietary guidelines (US), 419  
 dietary patterns, 418-419  
 dietary recommendations, 57-65, 60t-61t, 419-420  
   alcohol, 60t, 64-65, 419  
   carbohydrates, 59-62, 60t  
   fat substitutes, 64  
   fats, 25, 59, 60t, 419, 421  
   fiber, 62  
   fructose, 63  
   protein, 58-59, 436  
   salt, 60t  
   sucrose (sugar), 61t, 62-63, 419  
   sweeteners, 63-64  
 for dyslipidemia, 419-420, 421  
 exercise combined with, 53-54, 461-462, 462t  
 for hypertension, 407  
 individualization of plan for, 420  
 low-salt, 407  
 Mediterranean-style, 59  
 saturated fats, 59, 60t  
 USDA Dietary Guidelines, 60t-61t
- Dietician, 54
- Dipeptidyl peptidase-IV inhibitors. See *DPP-IV inhibitors*.
- Diuretics, 409t, 410t, 436
- Domperidone, 439-440
- Dopamine receptor agonist, 84t, 223-226. See also *Bromocriptine mesylate*.  
 Doxazosin, 411
- DPP (Diabetes Prevention Program) trial, 91, 462t, 463-464
- DPP-IV inhibitors (alogliptin; linagliptin; saxagliptin; sitagliptin), 84t-85t, 97-144. See also *specific agents*.  
 action mechanism, 97  
 advantages of, 141-142  
 agents, 84t-85t  
   alogliptin (Nesina), 84t, 127-141  
   linagliptin (Tradjenta), 85t, 119-126  
   saxagliptin (Onglyza), 85t, 109-118  
   sitagliptin (Januvia), 98-108  
 in algorithm for treatment, 358  
 combination agent with SGLT2 inhibitor (empagliflozin/linagliptin), 85t, 126-127  
 combination agent with thiazolidinedione, Oseni (alogliptin/pioglitazone), 85t, 140-141  
 combination agents with metformin, 85t, 94, 108-109  
   Janumet (sitagliptin/metformin), 85t, 108-109  
   Janumet XR (sitagliptin/metformin XR), 85t, 109  
   Jentadueto (linagliptin/metformin), 85t, 126  
   Kazano (alogliptin/metformin), 85t, 140  
   Kombiglyze XR (saxagliptin/metformin XR), 85t, 118  
 compared with SFUs, 97-98  
 dosing, 84t-85t  
 efficacy and safety trials. See *specific agents*.  
 indications for, 98, 358  
 renal disease, use in, 107-108, 117  
 summary, 141-142
- DREAM trial, 29, 462t, 465-466
- DRS study, 429
- DUAL trials, 338-339
- Duetact (pioglitazone/glimepiride), 88t, 184-185, 191-192
- Dulaglutide (Trulicity), 323-329  
 in algorithm for treatment, 358  
 cautions and contraindications, 328-329  
 dosage and administration, 297t, 329  
 efficacy, 323-328, 324t-325t  
   combination therapy, 323, 326-328, 354t-355t  
   in combination with one OAD, 326-328  
   in combination with two OADs, 328  
   monotherapy, 323-326, 327  
 FDA approval of, 287  
 indications for, 323  
 safety and tolerability, 328-329  
 weight changes and, 326, 327
- Dymelor. See *Acetohexamide*.
- Dyslipidemia, 413-423, 414t. See also *Cholesterol levels; Lipid levels; and specific classes of lipids*.  
 cardiovascular risk and, 413, 414t  
 characteristic abnormalities, 413, 414t  
 cholesterol measurements, 414-418  
 diet recommendations, 419-420, 421  
 lipid levels, 414t, 418  
   apoB, 414t  
 goals, 417t, 419

- Dyslipidemia, lipid levels (*continued*)  
 HDL-C, 413, 414t, 418  
 LDL-C, 413-414, 414t  
 lipid-lowering drugs, 417, 420-423, 421t  
 risk factors and, 421t  
 statins, 51, 417, 420-421, 421t, 422t, 470t  
 screening for, 414  
 treatment recommendations, 51, 414, 418, 420-423  
 lifestyle modifications, 418-420  
 triglycerides, 413
- Ear infections, 403t
- Early detection and management. See also *Prevention of type 2 diabetes*.  
 benefits of, 29, 41, 81  
 complications, reduction in, 29, 51, 425-426  
 disease progression, prevention/slowing of, 472  
 importance of, 20, 81, 425-426
- EDITION trials, 271
- Education. See *Patient education*.
- Elderly patients, 383  
 cautions in, 159, 169, 237, 400  
 hyperosmolar hyperglycemic syndrome vulnerability, 394  
 hypoglycemia susceptibility, 279, 367  
 insulin therapy in, 237  
 T1D in, misdiagnosis, 385
- EMPA-REG-OUTCOME trial, 176-178, 177, 423, 433-435
- Empagliflozin (Jardiance), 86t, 167-178  
 action mechanism, 168  
 in add-on or combination therapy, 168-169, 170t-171t  
 with insulin, 171t  
 adverse events, 169, 175t, 178  
 body weight, effects on, 168, 174  
 cardiovascular outcomes, 175, 176-178, 177, 423  
 combination agents  
 with linagliptin (Glyxambi), 85t, 126-127, 128  
 with metformin (Synjardy, Synjardy XR), 86t  
 dosage, 86t, 178  
 efficacy, 168-169, 170t-171t, 172, 173  
 EMPA-REG-OUTCOME trial, 176-178, 177, 423, 433-435  
 indications for, 167  
 prescribing information, 178  
 in renal impairment, 171t, 176, 178, 433-435  
 safety, 169, 178
- Endocrinopathies, 32t, 386t
- Environmental factors in type 2 diabetes, 23
- Erectile dysfunction (ED), 441-444, 443t  
 causes of, 441-442  
 defined, 441  
 diagnosis, 441  
 prevalence of, 441  
 treatments  
 avanafil (Stendra), 442, 443t  
 intracavernosal injection, 443  
 Medical Urethral System for Erection (MUSE), 443  
 penile prostheses and other therapies, 443-444
- Erectile dysfunction (ED), treatments (*continued*)  
 phosphodiesterase-5 (PDE-5) inhibitors, 442-444, 443t  
 sildenafil (Viagra), 442, 443t  
 tadalafil (Cialis), 442, 443t  
 testosterone, 442  
 vardenafil (Levitra), 442, 443t
- Erythromycin, 439
- ETDRS study, 429
- Ethnicity. See *Race/ethnicity*.
- Etiology of type 2 diabetes, 23-27
- European Association for the Study of Diabetes (EASD), 357
- Evolocumab, 421-422
- EXAMINE study, 138
- Exenatide (Byetta), 287-299  
 in algorithm for treatment, 358  
 body weight effects, 291, 291, 292-293, 292, 294, 295, 296  
 combination therapy  
 with metformin, 287-289, 288t  
 with SFUs, 287, 288t  
 with TDZs, 289  
 dosage and administration, 295-299, 297t  
 efficacy  
 $\beta$ -cell function, 293  
 CV risk factors, 295  
 glycemic control, 287-295  
 extended-release formulation (Bydureon), 295-299  
 contraindications, 299  
 efficacy and safety, 295-298, 298t  
 prescribing, 298-299  
 FDA approval of, 286  
 indications for, 287, 358  
 side effects, 291-292  
 hypoglycemia, 291-292, 293  
 trials and studies of, 287-295  
 comparative and long-term open-label trials  
 82-week studies, 293-295, 294  
 exenatide vs insulin glargine, 290-293, 292  
 HEELA, 292-293  
 phase 3 clinical trials, 287-289, 288t, 290-291  
 vs liraglutide, 308, 310
- Exercise, 67-69, 355, 357  
 aerobic, recommendations, 69  
 benefits of, 67, 462t  
 combined with diet, 53-54, 461-462, 462t  
 as first line therapy, 29, 53-54  
 diabetes prevention and, 462t  
 glucose monitoring and, 69t  
 guidelines/prescription, 68-69, 69t, 70t  
 hypoglycemia induced by, 68, 396-397, 400  
 ID badge, carrying, 69t  
 lack of (sedentary lifestyle), 19, 25, 27, 37, 42, 406  
 medical exam/stress test before, 67  
 precautions and considerations, 67-68  
 recommendations, 61t, 69, 69t, 70t, 406  
 safety in, 67, 69, 69t  
 self-monitoring of blood glucose and, 400

- Eyes, 425-430. See also *Diabetic retinopathy*.  
 blurred vision, 41, 400  
 eye exams, 425-426, 428, 429t  
 retinal detachment, 68  
 Ezetimibe, 417
- Farxiga. See *Dapagliflozin*.
- Fasting plasma glucose, 238, 363. See also *Glycemic control; specific agents*.  
 as diagnostic criterion, 16, 43-44, 43t, 358  
 impaired (IFG), 33t  
 target/goal levels, 44, 74t, 356t, 362t  
 testing for, 28, 42, 44, 363
- Fat  
 body fat distribution, 27, 37. See also *Obesity; Weight*.  
 cells, increased lipolysis in, 25, 72  
 dietary, 25, 59, 60t, 419  
   incidence of diabetes and, 25  
   recommendations for, 49, 59, 60t, 419, 421  
   substitutes, 64
- Fatigue, 383, 400
- FDPS (The Finnish Diabetes Prevention Study), 462-463, 462t
- Fiber, dietary, 62
- Fibrates, 51, 417, 421, 421t
- Fingerstick devices, 373-379
- Finnish Diabetes Prevention Study (FDPS), 462-463, 462t
- Fish oil, 421
- Fludrocortisone, 440
- Foot disorders in diabetes, 444-445, 446t
- Foot drop, 438
- Fortamet, 84t, 94. See also *Metformin (MET)*.
- FPG. See *Fasting plasma glucose*.
- Framingham Study, 413
- Fructosamine measurement, 365, 365, 371
- Fructose, 63
- GAD. See *Glutamic acid decarboxylase*.
- Gastric emptying, 284, 343
- Gastroparesis, 439-440
- GDM. See *Gestational diabetes mellitus (GDM)*.
- GEMINI study, 411
- Genetic syndromes, diabetes secondary to, 33t
- Genetics, 23, 26, 34-35  
   thrifty gene hypothesis, 18-19  
   twin studies, 23, 34-35
- Gestational diabetes mellitus (GDM), 32t, 35-36  
 as risk factor for type 2 diabetes, 41  
 screening for, 44
- GetGoal-Duo 1 trial, 341
- Gila monster, 287
- GIP (glucose-dependent insulinotropic polypeptide), 97, 283
- Glargine (Lantus), 229, 245, 266-269, 469. See also *Insulin therapy*.  
 Basaglar U-100 (insulin glargine follow-on biologic), 269  
   efficacy, 269-270  
   starting or switching to, 270  
   efficacy, 267-268
- Glargine (Lantus) (*continued*)  
 fixed-dose combination agent: glargine/lixisenatide (Soliqua 100/33), 340-342  
 glargine U-100, 229, 266-269  
 glargine U-300 (Toujeo), 229, 245, 270-271, 272t  
   time course of action, 233t, 235  
   hypoglycemia and, 245, 268-269  
 ORIGIN trial, 468, 470t  
 safety, 268-269  
 switching to and from, 268  
 time course of action, 233t, 235
- Glimepiride (Amaryl), 87t, 203, 205-206. See also *Sulfonylureas*.  
 combination formulations  
   with pioglitazone (Duetact), 88t  
   with rosiglitazone (Avandaryl), 88t, 181  
 combination therapy  
   with liraglutide, 303-304  
   with sitagliptin, 104  
 dosage, 87t, 205  
   for Avandaryl and Duetact, 88t
- Glinides, 85t, 209-215. See also *Nateglinide; Repaglinide*.  
 combination agent with biguanide (metformin), 85t, 211  
 dosing/prescription considerations, 85t  
 side effects, 211, 213-214
- Glipizide (Glucotrol), 87t, 203, 206. See also *Sulfonylureas*.  
 combination therapy  
   with metformin (Metaglip), 87t, 94-95  
   with sitagliptin, 101-104  
 dosing, 87t, 206  
 extended release (Glucotrol XL), 87t, 206
- Glipizide/metformin (Metaglip), 87t, 94-95. See also *Glipizide; Metformin*.
- GLP-1 (glucagonlike peptide 1), 97, 283-286, 284. See also *DPP-IV inhibitors; GLP-1 analogues*.  
 degradation by DPP-IV, 286, 313  
 exogenous, administration of, 284-285, 285  
 gastric emptying and, 284  
 half-life, 286  
 weight effects of, 286
- GLP-1 analogues, 286-342. See also *specific agents*.  
 agents  
   albiglutide (Tanzeum), 313-323  
   dulaglutide (Trulicity), 323-329  
   exenatide (Byetta), 287-299  
   liraglutide (Victoza), 299-313  
   lixisenatide (Adlyxin), 329-337  
 in algorithm for treatment, 358  
 approved by FDA, 286-287  
 dosing information, 297t  
 fixed-combination products with basal insulin, 338-342  
   insulin degludec/liraglutide (Xultophy 100/3.6), 338-340  
   insulin glargine/lixisenatide (Soliqua 100/33), 340-342  
 indications for, 287, 299, 313, 323, 329, 337  
 resistance to DPP-4 degradation, 286, 287  
 summary, 337

- Glucagon, 72, 73, 109, 284. See also *GLP-1 (glucagonlike peptide 1); GLP-1 analogues*.  
 amylin/pramlintide and, 284, 343  
 intramuscular injection for severe hypoglycemia, 398-399  
 Glucagon secretion, increased, 23, 24, 72  
 Glucagonlike peptide. See *GLP-1*.  
 Glucophage (metformin), 84t. See also *Metformin (MET)*.  
 Glucophage XR, 84t, 93. See also *Metformin (MET)*.  
 Glucoregulatory hormones, 283-354. See also *GLP-1 analogues; Pramlintide*.  
 amylin analogue (pramlintide), 343-350  
 GLP-1 analogues, 286-342  
 incretins, 283-286  
 insulin. See *Insulin*.  
 multihormonal control of glucose homeostasis, 284  
 Glucose-dependent insulinotropic polypeptide. See *GIP*.  
 Glucose levels, 42-44, 355. See also *Glycemic control; Plasma glucose concentration (PGC); Postprandial glucose (PPG)*.  
 assessment of, 361-363  
 in diagnosis, 42-44, 43t  
 glucose homeostasis, multihormonal control of, 284  
 intensive control of, CV risk and, 75-80  
 monitoring. See *Glucose monitoring*.  
 multihormonal control of, 284  
 normal, 42t  
 targets/goals for, 74t, 80, 362t  
 Glucose monitoring, 361-380. See also *Glucose levels; Glycemic control; Self-monitoring of blood glucose (SMBG)*.  
 advances in, 373-380  
 approaches to glucose testing, 42-44  
 checking before bedtime, 400  
 continuous glucose monitoring systems, 379-380  
 interstitial vs plasma glucose measurement, 379-380  
 self-monitoring of blood glucose, 366-373  
 Glucose production, hepatic  
 insulin therapy and, 228  
 in pathogenesis of type 2 diabetes, 23, 24, 25, 37t, 72  
 in transition from IGT to type 2 diabetes, 23-25, 26, 27  
 Glucose reabsorption, hepatic, 23, 24, 72  
 Glucose tolerance, impaired. See *Impaired glucose tolerance*.  
 Glucose toxicity, 384, 385  
 Glucotrol, Glucotrol XL. See *Glipizide*.  
 Glucovance (glyburide/metformin), 87t, 94. See also *Glyburide; Metformin*.  
 Glulisine (Apidra), 228, 258-259  
 time course of action, 231, 232t, 235, 258  
 Glumetza, 84t, 93. See also *Metformin (MET)*.  
 Glutamic acid decarboxylase (GAD) antibodies, 34, 228, 250  
 Glyburide (DiaBeta, Micronase, Glynase PresTab), 87t, 203, 206. See also *Sulfonylureas*.  
 combination formulation with metformin (Glucovance), 87t, 94  
 combination therapy  
 with alogliptin, 135t, 137  
 with saxagliptin, 112-114  
 dosing considerations, 87t, 206  
 Glynase PresTab (micronized formulation), 87t, 203  
 Glyburide/metformin (Glucovance), 94  
 Glycated hemoglobin assay/measurement, 363-364. See also *Glucose monitoring; Glycosylated hemoglobin (A1C)*.  
 Glycated proteins, measurement of, 364-365  
 Glycation, defined, 363  
 Glycemic control. See also *Glucose levels; Glucose monitoring; specific treatments and agents*.  
 in algorithm for treatment, 355, 358  
 assessment of, 361-363  
 during office visits, 361  
 self-monitoring of blood glucose, 366-373  
 benefits of, 74-75, 75t, 76, 81  
 importance of, 357, 366, 379, 405-406, 426  
 intensive therapy for, 74-80  
 targets/goals for, 74t, 80, 356t, 418  
 Glycosylated hemoglobin (A1C), 31, 37t, 42-44, 363-364. See also *specific treatments and agents*.  
 in diagnosis, 42-44, 42t, 43t, 358  
 false lows and highs, 364  
 home measurement kits, 364  
 hyperglycemia and, 363  
 measurement of, 363-364  
 normal value, 42t  
 other glycated proteins and, 364-365, 365  
 regularity of monitoring, 364  
 in screening, 28  
 targets/goals for, 74t, 80, 362t, 406  
 Glynase PresTab (glyburide), 87t, 203. See also *Glyburide*.  
 Glyset. See *Miglitol*.  
 Glyxambi (empagliflozin/linagliptin), 85t, 126-127, 128  
 Gut hormones. See *Incretins*.  
 HDL (high-density lipoprotein), 415  
 cholesterol (HDL-C), 413, 414t  
 CV risk and, 49  
 raising, 421t, 423  
 target/goal level, 362t, 418, 419  
 measurement, 415  
 pioglitazone and, 185  
 small HDL, 414t  
 HEART2D trial, 279  
 HEELA study, 292-293  
 Hepatic glucose production. See *Glucose production, hepatic*.  
 Hepatic glucose reabsorption, 23, 24, 72  
 High-density lipoprotein. See *HDL*.  
 Hispanic/Latino Americans. See also *Race/ethnicity*.  
 prevalence of diabetes in, 15, 17, 18  
 risk of diabetes in, 41  
 HMG-CoA reductase inhibitors. See *Statins*.  
 Home monitoring. See *Self-monitoring of blood glucose*.  
 HOPE trial, 408-410, 470t  
 Hormones. See *Glucoregulatory hormones*.  
 HPS study, 413  
 Humalog (lispro), 228, 255-257  
 premixed preparation, 229  
 time course of action, 230, 232t



- Humalog Mix  
 Humalog Mix 50/50, 233t, 244, 249, 275  
 Humalog Mix 75/25, 233t, 244, 275  
 time course of action, 233t
- Human insulin, 228, 229. See also *Insulin therapy*.
- Humulin, 229, 263-266  
 Humulin 70/30, 50/50, 233t, 275  
 Humulin R U-100, 264  
 Humulin R U-500, 264-266, 270
- Hyperglycemia, 23, 24, 37, 355  
 aggressive management of, 71  
 avoiding, with SMBG, 367  
 cardioprotective benefits of pharmacologic therapy for, 423  
 diabetic ketoacidosis and, 384, 385, 387  
 diabetic retinopathy and, 74  
 fasting, 23  
 HHS and, 394  
 increase in glycosylated hemoglobins with, 363  
 insulin resistance and, 71  
 insulin therapy for, temporary, 71  
 postprandial, 73-74  
   importance of controlling, 73-74  
   target PPG levels, 74t  
 premeal, techniques to adjust for, 372t  
 renal insufficiency and, 431  
 severe, 367  
 signs and symptoms of, 41, 358
- Hyperinsulinemia, 25, 227
- Hyperosmolar hyperglycemic syndrome (HHS), 394-396  
 diagnosis, 395  
 laboratory evaluation, 389t, 395  
 life-threatening nature of, 394  
 symptoms and signs of, 389t, 394-395  
 treatment of, 395-396
- Hypertension, 42, 406-412  
 antihypertensive drugs, 407-412, 409t  
 ACE inhibitors and ARBs, 408-411  
 benefits of, 407-408, 410t, 426  
 choice of, 412  
 complications of, 409t  
 multiple-drug therapy, 408  
 prevention or delay of T2D complications, 426  
 SGLT2 inhibitors as, 408  
 home vs office measurement (white coat hypertension), 407  
 masked hypertension, 407  
 as risk factor  
   for cardiovascular disease, 48, 406  
   for renal disease, 431, 432-433  
 treatment of, 407-412  
   antihypertensive drugs, 407-412, 409t  
     new-onset diabetes and, 411, 470  
   benefits for nephropathy, 435-436  
   diet, 407  
 trials and studies  
   HOPE, 408-410  
   SPRINT, 407
- Hypertriglyceridemia. See *Dyslipidemia; Triglycerides*.
- Hypoglycemia, 396-400  
 ADA definition of, 396  
 causes of, 396-397  
 detection and prevention with SMBG, 367  
 emergency treatment kits for family members, 398-399  
 exercise and, 68, 396-397, 400  
 mild, moderate, and severe, 398-399  
 nocturnal, 245, 274-275, 279, 291-292, 293  
   checking blood glucose before sleep, 400  
 patient education on, 399-400  
 prevention of, 399-400  
 recognizing symptoms of, 355  
 severe, 398-399  
 as side effect  
   of ACE inhibitors, 410  
   of alogliptin, 139  
   of bromocriptine mesylate, 224  
   of empagliflozin, 169  
   of exenatide, 291-292, 293  
   of insulin therapy, 268-269, 279  
   of lixisenatide, 331  
   of metformin combinations, 91  
   of nateglinide, 213  
   of pramlintide, 348-349  
   of SFUs, 204, 205  
   of sitagliptin, 107  
   of Xultophy 100/3.6, 340  
 signs and symptoms of, 397-398  
 treatment of, 398-399  
 type 1 diabetes, 279
- Hypotension, 407  
 orthostatic, 411, 440
- IFG. See *Impaired fasting glucose*.
- IGT. See *Impaired glucose tolerance*.
- Impaired fasting glucose (IFG), 33t
- Impaired glucose tolerance (IGT), 23-26  
 characteristics of, 23  
 obesity and, 449  
 prevalence of, 461  
 transition to type 2 diabetes, 23-26  
 trials and studies, Da Qing IGT and Diabetes Study, 461-462, 462t
- Impotence. See *Erectile dysfunction*.
- Incidence of diabetes, 16-18, 16, 20  
 by age, 15, 16, 20, 21, 35  
 increase in, 15, 19, 21  
 by race/ethnicity, 15, 17
- Incretin effect, 24, 25, 72, 97, 283
- Incretin mimetics. See *GLP-1 analogues*.
- Incretins, 283-286, 284. See also *Amylin; DPP-IV inhibitors; GLP-1 analogues*.  
 DPP-IV inhibitors and, 97
- Indapamide, 436
- Indian Health Services (IHS), 480
- Indians, American. See *American Indians*.

- Infections, 41, 400, 402t-403t  
 diabetic ketoacidosis and, 386t
- Insulin. See also *Insulin resistance*; *Insulin therapy*.  
 action mechanism, 228, 284  
 deficiency  
   β-cell exhaustion and, 227-228  
   in diabetic ketoacidosis, 383-384, 385  
 diurnal variations in, 238-240  
 multihormonal control of, 284  
 types of insulin, 228
- InsulinDependence, Inc., 481
- Insulin-dependent diabetes. See *Type 1 diabetes (T1D)*.
- Insulin receptor abnormalities, 33t
- Insulin resistance, 23, 26, 42, 48, 71, 72. See also *Metabolic syndrome*.  
 antidiabetic treatment and, 26  
 cardiovascular disease and, 48  
 compensated, 25-26  
 in continuum of prediabetes to diabetes, 27-28, 27  
 factors influencing, 48, 49  
 hyperglycemia and, 71  
 obesity and, 49, 449  
 present prior to diabetes diagnosis, 25  
 in transition from IGT to type 2 diabetes, 25, 26, 27-28, 27
- Insulin secretion, impaired, 23, 24, 25, 26, 72
- Insulin therapy, 227-282, 355. See also *specific formulations/preparations of insulin*.  
 in algorithm for treatment, 358  
 backups for interruption of, 393  
 basal, 229, 232t-233t, 238, 239  
 benefits of, 227  
 combination therapy, 238-244, 358  
   with alogliptin, 135t, 137  
   benefits of, 239-240  
   dosing guidelines/calculation, 242t, 243t  
   dose adjustment with SMBG, 241, 242t  
   patient selection for, 237-238, 240  
   patient self-adjustment with SMBG, 241, 242t, 372-373, 372t, 376-377, 378t  
   rationale for, 239-241  
   with sitagliptin, 104-105  
 complications of, 278-279  
   hypoglycemia, 268-269, 279  
   weight gain, 278-279  
 for diabetic ketoacidosis, 388, 391, 392-393  
 dosage, adjustment via SMBG data, 241, 242t, 372t  
 hypoglycemia, 268-269, 279. See also *Hypoglycemia*.  
   nighttime, 274-275, 279  
 inadequate, diabetic ketoacidosis and, 384-385, 386t  
 indications for, 227-228  
   diabetic ketoacidosis, 384-385, 391  
   temporary correction of hyperglycemia, 71  
   temporary therapy prior to other OADs, 20  
   type 1 diabetes, 34  
 initiation of, 227, 246-248
- Insulin therapy (*continued*)  
 insulin preparations  
   fast-acting analogues, 228, 230-231, 231, 255-263  
   aspart (Novolog), 228, 230, 232t, 257-258  
   glulisine (Apidra), 228, 231, 232t, 258-259  
   lispro (Humalog), 228, 230, 232t, 255-257  
   regimens using, 229  
   time course of action, 230-231, 232t, 235, 257  
 human insulin, 228  
 inhaled insulin (Afrezza), 232t, 235, 259-263  
 intermediate-acting (NPH), 229, 232t  
 long-acting insulins, 229, 266-270  
   detemir (Levemir), 229, 233t, 266  
   glargine (Lantus), 229, 233t, 266-269  
   time course of action, 233t  
   newer preparations, 255-278  
   Afrezza (inhaled insulin), 259-263  
   aspart (Novolog), 257-258  
   Basaglar U-100 (insulin glargine follow-on biologic), 269  
   detemir (Levemir), 266  
   glargine U-100, 266-269  
   glulisine (Apidra), 228, 258-259  
   lispro (Humalog), 255-257  
   long-acting insulins, 266-270  
   premixed formulations, 229, 275-278  
   short-acting (regular human insulin), 263-266  
   ultralong-acting insulins, 270-275  
 premixed, 229, 244, 248, 275-278  
   advantages of, 276  
   biphasic insulin, 233t-234t  
   disadvantage of, 276, 278-279  
   dosing, 242t, 243t  
   Humalog (lispro protamine suspension + lispro injection), 229  
   Humalog Mix 50/50 (lispro), 233t, 244, 249, 275  
   Humalog Mix 75/25 (lispro), 233t, 244, 275  
   human insulin isophane suspension + injection (Humulin or Novolin), 229, 232t  
   Humulin, 229, 263-266  
   Humulin 70/30, 50/50, 233t, 275  
   Novolin (aspart protamine + aspart injection), 229  
   Novolin 70/30 (NPH-insulin), 233t, 275  
   Novolog, 229  
   Novolog Mix 50/50, 70/30 (aspart), 244, 275  
   Ryzodeg 70/30, 229, 233t, 244, 275, 276-278, 358  
   time course of action, 233t-234t, 275  
 selection of, 228-231  
   time course of action and, 229-231, 232t-234t, 235  
 short-acting (regular human insulin), 229, 263-266  
   time course of action, 232t  
 short/fast-acting, 229  
 time course of action, 229-231, 232t-234t  
   peak action, 235  
 ultralong-acting insulins, 229, 270-275  
   degludec U-100 and U-200 (Tresiba), 229, 233t, 271-275  
   glargine U-300 (Toujeo), 229, 233t, 270-271  
   time course of action, 233t

- Insulin therapy (*continued*)
- intensive therapy, 237-238
    - initiation of, 249
    - patient selection for, 237-238
  - in obese patients, 248-249
  - ORIGIN trial, 268, 468, 470t
  - pump therapy, 236t, 249-251
    - in algorithm for treatment, 358
    - reduced insulin usage with, 252, 254, 256
    - Tandem t:flex insulin pump, 252-255
    - V-Go device, 251-252, 251, 253, 254, 255t, 256
  - regimens for, 229, 236t, 239, 358
    - basal bolus, 238, 239, 242t, 243t, 245, 248
    - basal insulins, 229, 232t-233t, 235, 238, 239, 245, 270
      - calculation of doses, 241, 242t, 243t
      - dose adjustments, 241, 242t
    - bolus insulin, 229
    - combination therapy, 238-244
    - fast-acting insulins, 229, 232t, 245, 358
    - initiating and changing, 243t, 246-248
    - insulin and oral agents, 236t
    - mealtime insulins, 232t
    - multiple-injection, 236t, 244-248, 358
      - multiple-daily-injection (MDI), 245
    - premixed insulin, 242t, 244, 248, 275-278
    - progression in, 238, 239, 246
    - pump therapy, 236t
    - self-titration algorithms (Q1D, Q3D), 246, 247t
    - short-acting insulin in, 229
    - single-injection, 236t
    - split-mixed, 249, 358, 373, 378t
    - ultralong-acting, 270-275
  - selection of insulin preparation, 228-231
  - self-monitoring of blood glucose (SMBG), dosage adjustment and, 241, 242t, 249
    - in thin patients, 248-249, 279
  - time course of action of insulin preparations, 229-231, 230-231, 232t-234t
    - mimicking normal insulin delivery, 229
    - peak action, 232t-234t, 235
    - timing of initiation (of insulin therapy), 227-228
    - timing of insulin doses (during the day), 231, 372t
  - Intensive therapy for Type 2 diabetes, 74-80, 237-238
    - benefits of, 20, 74, 75t, 78
    - questions about, 79-80
    - CV risk and, 75-80
    - intensive insulin therapy, 237-238, 249. See also *Insulin therapy*.
    - reduced complications with, 74-75, 75t
  - International Diabetes Federation (IDF), 480-481
  - Intestinal peptides, 283, 284. See also *Incretins*.
  - Invokamet, Invokamet XR (canagliflozin/metformin), 86t
  - Invokana. See *Canagliflozin*.
  - IRIS study, 469, 470t
  - Islet cell antibody (ICA), 228
  - Janssen Pharmaceuticals. See also *Canagliflozin (Invokana)*.
  - Janumet (sitagliptin/metformin), 85t, 108-109
  - Janumet XR (sitagliptin/metformin XR), 85t, 109
  - Januvia. See *Sitagliptin*.
  - Jardiance. See *Empagliflozin*.
  - Jentadueto (linagliptin/metformin), 85t, 126
  - Joslin Diabetes Center, 481
  - Juvenile Diabetes Research Foundation (JDRF), 482
  - Kazano (alogliptin/metformin), 85t, 140
  - Ketoacidosis. See *Diabetic ketoacidosis*.
  - Ketones, serum, 365, 387
  - Ketosis, 394. See also *Diabetic ketoacidosis*.
  - Kidney disease, 431-436. See also *Diabetic nephropathy; Renal function*.
    - chronic (CKD), 434-435, 434t
      - empagliflozin for, 434-435
    - Kidney function. See *Renal function*.
  - Kidney impairment, metformin and, 93
  - Kombiglyze XR (saxagliptin/metformin XR), 85t, 118
  - Kussmaul's respiration, 385-387, 395
  - LADA (latent autoimmune diabetes in adults), 32t, 34, 228, 250
  - Lantus. See *Glargine*.
  - Latent autoimmune diabetes in adults (LADA), 32t, 34, 228, 250
  - Latino Americans. See *Hispanic/Latino Americans*.
  - LDL (low-density lipoprotein), 414, 414t
    - cholesterol (LDL-C), 413, 414t
      - altered characteristics of particles, 413-414
      - glycosylation, 414
      - high, cardiovascular risk and, 48
      - measurement, 415
      - target/goal levels, 49, 362t, 415, 417t, 419, 420
  - LDL-P, 416-417, 417t
  - lowering, 417t, 420-423, 421t
    - add-on therapies, 421-422
      - with bile acid sequestrants, 421t
      - with fibrates, 421t
      - with HMG-CoA reductase inhibitors, 421t
    - lifestyle therapy, 417, 418-420
      - with metformin, 92
      - with nicotinic acid, 421t
      - with PCSK-9 inhibitors, 421-423, 421t
        - with statins, 417, 420-421, 421t, 422t
    - particle number and characteristics, 414, 414t, 416, 417t
    - pioglitazone and, 185
    - small dense LDL, 414t
    - VLDL (very low-density lipoprotein), 413
  - LEAD trials, 299-309, 301t-302t, 303t
  - LEADER trial, 309-313, 312, 423
  - Lean type 2 diabetic patients, 72
  - Lethargy, 383, 387
  - Levemir. See *Detemir*.
  - Levitra (vardenafil), 442, 443t
  - LIFE study, 411

- Lifestyle modifications, 29, 49, 61t, 367-368, 418-420. See also *Diet; Exercise; Nutrition*.
- as initial treatment approach, 49, 83, 358
  - combined with metformin, 83
  - pharmacologic therapy as adjunct to, 71, 83
- Lifestyle, sedentary, as risk factor for diabetes, 19, 26, 27, 37, 42, 406
- Linagliptin (Tradjenta), 85t, 119-126
- adverse events, 125
  - cardiovascular outcomes, 123
  - combination formulation
    - with empagliflozin (Glyxambi), 85t, 126-127, 128
    - with metformin (Jentadueto), 85t, 126
  - combination therapy, 119, 121-123
    - with metformin, 121, 122
    - with metformin and SFU, 122-123, 124t
    - with pioglitazone, 123
    - with SFU, 121-122
  - dosage, 85t, 125-126
  - efficacy, 119-123, 125
  - indications for, 119
  - pharmacokinetics, 119
  - prescribing information, 125-126
  - trials
    - combination or add-on treatment, 121-123
    - long-term treatment, 125
    - monotherapy, 119-121, 120
- Lipid levels, 413-423. See also *Dyslipidemia; HDL; LDL; Triglycerides*.
- colesevelam and, 217
  - diet and, 419-420, 421
  - goals for, 362t, 414, 417t, 419
  - HDL-C, 413, 414t, 419
  - LDL-C, 413, 414t
  - lipid abnormalities in diabetic patients, 413-414, 414t
  - metformin and, 91-92
  - pharmacologic agents, lipid-lowering, 417, 420-423, 421t, 422t
  - phenotype B pattern, 413
  - pioglitazone and, 185
  - triglycerides, 413, 414t
- Lipoprotein A, 414t, 423
- Liraglutide (Victoza), 299-313
- action mechanism, 299, 455
  - in algorithm for treatment, 358
  - cardiovascular outcomes (LEADER trial), 309-313, 312
  - combination therapy, 299
    - fixed-combination product with basal insulin (Xultophy 100/3.6), 338-340
      - with glimepiride, 303-304
      - with metformin, 299, 300t, 304, 306-308, 306t, 307
      - with rosiglitazone, 303-304, 305, 306-308, 307
      - with SFUs, 121-122, 299
      - with TZD, 299
  - contraindications and cautions, 313, 455-456, 457
  - dosage and administration, 297t, 311-313
    - of Saxenda (for obesity treatment), 457
  - FDA approval of, 287
  - indications for, 299, 313
- Liraglutide (Victoza) (*continued*)
- for obesity treatment (Saxenda), 455-457
  - safety and tolerability of, 308-309
- Saxenda (for obesity treatment), 455-457
- warnings and cautions, 455-456, 457
  - trials and studies of, 299-308
    - LEADER (CV outcomes), 309-313, 312, 423
    - phase 3 clinical trials, 299-308, 300t-301t
      - in combination with one OAD, 300t, 303-304, 305
      - in combination with two OADs, 301t, 306-308, 307
    - LEAD trials, 299-309, 301t-302t, 303t
      - monotherapy (LEAD-3), 301t, 302-303, 303t
      - with rosiglitazone, 303-304, 305, 306-308, 307
    - vs exenatide, 308, 310
    - vs glimepiride, 302-303, 303t
- Lisinopril, in ALLHAT, 412, 470t
- Lispro (Humalog), 228, 255-257. See also *Humalog; Humalog Mix*.
- time course of action, 230, 232t, 235, 257
  - U-100 and U-200, 228, 257
- Liver function, 192-193
- LixiLan-L trial, 341, 342
- LixiLan-O trial, 341-342
- LixiLan Proof-of-Concept trial, 341
- Lixisenatide (Adlyxin), 329-337
- action mechanism, 329-330
  - in combination therapy, 330-336
  - contraindications, 337
  - dosage and administration, 336-337
  - efficacy, 330-336, 332t-335t
    - in combination with basal insulin, 331-336
    - in combination with MET, 330-331
    - in combination with SFU or pioglitazone, 331
  - monotherapy, 330
  - FDA approval of, 287, 329
  - fixed combination product with insulin glargine (Soliqua 100/33), 340-342
  - indications for, 329
  - safety and tolerability, 336
- Loop diuretics, 436
- Lorcaserin (Belviq), 451-453
- Low-density lipoprotein. See *LDL*.
- Low-density lipoprotein cholesterol. See *LDL-C*.
- Macrovascular disease, 405-424. See also *Cardiovascular outcomes*.
- pioglitazone, in PROactive Study, 188-190, 190, 191
- Malnutrition-related diabetes mellitus, 32t
- Maturity-onset diabetes of the young (MODY), 38
- Medical evaluation (Diabetes Warranty Program), 45, 46-47
- Meglitinide, 209-211. See also *Repaglinide (Prandin)*.
- MET. See *Metformin*.
- Metabolic abnormalities in T2D, 23-25, 24, 27-28, 27, 72
- correctable with insulin therapy, 228
  - goals for treatment, 49, 355
- Metabolic complications of T2D, 383-400. See also *Complications of diabetes*.
- Metabolic control. See *Glycemic control*.
- Metabolic goals of treatment, 49, 355, 362t

- Metabolic syndrome, 49-51, 50t  
 diagnostic criteria for, 49, 50t  
 IDF definition, 49-51, 50t  
 recommended treatment, 51  
 risk factors for, 48
- Metaglip (glipizide/metformin), 87t, 94-95
- Metformin (MET), 84t, 91-95  
 action mechanism, 91  
 in algorithm for treatment, 358  
 benefits of, 51, 91-92  
 combination formulations, 85t-88t  
   with alogliptin (Kazano), 85t, 140  
   with glipizide (Metaglip), 87t, 94-95  
   with glyburide (Glucovance), 87t, 94  
   with linagliptin (Jentadueto), 85t, 126  
   with pioglitazone (Actoplus Met/Actoplus Met XR), 88t, 184, 186t-187t  
   with repaglinide (PrandiMet), 85t, 211  
   with rosiglitazone (Avandamet), 88t, 181  
   with saxagliptin (Kombiglyze XR), 85t, 118  
   with SGLT2 inhibitors, 86t  
   with sitagliptin (Janumet), 85t, 108-109  
 combination therapy, 94-95, 358  
   with alogliptin, 129-131, 132t, 134t, 136-137  
   with canagliflozin, 147, 148t-149t  
   with DPP-4 inhibitors, 94  
   with empagliflozin, 168-169, 170t-171t  
   with exenatide, 287-289, 288t  
   with GLP-1 receptor agonists, 94  
   with linagliptin, 121, 122  
   with liraglutide, 299, 300t, 304, 306-308, 306t, 307  
   with lixisenatide, 330-331  
   with nateglinide, 212  
   with pioglitazone, 136-137, 182, 184  
   with repaglinide, 209-210, 210  
   with saxagliptin, 110-112, 111t, 113t, 114  
   with SFUs, 94-95  
   with SGLT2 inhibitors, 94  
   with sitagliptin, 98, 100-101, 102  
   with TDZs, 94  
 triple-combinations, 122-123, 210, 358  
 contraindications, 93  
 dosage/titration, 83, 84t, 93  
 effect on lipids, 91-92  
 extended-release formulation (Glucophage XR, Fortamet, Glumetza), 84t, 93  
 as initial therapy, 83, 358  
   concurrent with lifestyle interventions, 83, 360  
   upon diagnosis, 358, 360  
 prescribing considerations, 93-94  
 in prevention of diabetes, 29, 51, 472  
 safety, 92-93  
   with renal impaired patients, 92-93  
 side effects, 92  
   hypoglycemia, 91  
   lactic acidosis, 92
- Metformin (MET) (*continued*)  
 trials and studies  
   DPP, 91, 462t, 463-464  
   UKPDS, 91
- Metoclopramide HCl, oral, 439
- Microalbuminuria, 431  
 measurement of microalbumin, 365
- Microaneurisms. *See Diabetic retinopathy.*
- Micronase (glyburide). *See Glyburide.*
- Microvascular complications of diabetes, 425-448
- Microvascular disease, 425-448. *See also Complications of diabetes.*  
 prevention/reduction with glycemic control, 74-75, 75t, 357, 425
- Miglitol (Glyset), 84t, 200-202  
 combination therapy, 200-202, 210  
 dosage, 84t, 201t, 202  
 prescribing information, 201t, 202  
 side effects, 202
- Mineral supplementation, 61t, 64
- Monitoring of glucose levels. *See Glucose monitoring; Glycemic control.*
- Mononeuropathies, 438
- Monounsaturated fats, 419
- Morbidity and mortality. *See also Cardiovascular risk; Myocardial infarction.*  
 cardiovascular, diabetes and, 45-48, 181, 405, 406, 408  
 of diabetes, 19-20, 405  
 risk of, with diabetes, 19-20
- Mortality. *See Morbidity and mortality.*
- Myocardial infarction, 386t
- Naltrexone/bupropion (Contrave), 453-455
- Nateglinide (Starlix), 85t, 212-214  
 action mechanism, 212  
 dosage, 85t, 213  
 glycemic control with, 209-210, 212-213, 214  
 in NAVIGATOR trial, 468  
 prescribing information, 213  
 side effects, 213-214
- National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP), 479-480
- National Cholesterol Education Program (NCEP) guidelines, 48, 49
- National Diabetes Education Initiative (NDEI), 482
- National Diabetes Education Program (NDEP), 482-483
- National Eye Institute (NEI), 483
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), 483-484
- National Kidney Foundation, 484
- Native Americans. *See American Indians.*
- Natural history of type 2 diabetes, 27-29, 27t, 75, 227, 471
- NAVIGATOR trial, 468
- NCEP. *See National Cholesterol Education Program.*
- Nephropathy. *See Diabetic nephropathy.*
- Nesina. *See Alogliptin*
- Neurogenic bladder, 431, 440
- Neuropathies. *See Diabetic neuropathy.*
- Neurotransmitter dysfunction, 25, 72
- Neutral protamine Hagedorn (insulin). *See NPH.*

- NHANES, 413
- Niacin, 417
- Nisoldipine, 412
- Non-insulin-dependent diabetes. See *Type 2 diabetes (T2D)*.
- Nonpharmacologic treatment of type 2 diabetes, 53-69. See also *Exercise*;  
*Nutrition*.
- exercise, 67-69, 357
  - nutrition, 53-66
  - self-monitoring of blood glucose and, 370-371, 372t
- Novo Nordisk, 399
- Novolin, 229
- Novolin 70/30 (NPH-insulin), 233t, 275
- Novolog (aspart), 228, 229, 257-258
- regimens for, 249
  - time course of action, 230, 232t, 235, 257-258
- Novolog Mix 70/30, 50/50, 244, 249, 275
- time course of action, 233t
- NPH
- Novolin 70/30 (NPH-insulin), 233t, 275
  - time course of action, 232t, 233t, 235
- Nutrition, 53-66, 355, 357. See also *Diet*; *Weight*.
- alcohol intake, 60t, 64-65, 419
  - body weight considerations, 55-57, 56t
  - caloric intake, 55, 57-58
    - “spreading the calories,” 199
  - carbohydrates, 59-62, 60t
  - dietary guidelines (US), 419
  - dietary patterns, 418-419
  - dietician, nutrition consult with, 54
  - exercise combined with, 53-54
  - fat intake, 59, 60t
  - fat substitutes, 64
  - fructose in, 63
  - goals of, 53
  - individualization of plan for, 420
  - lipid levels and, 418-419
  - malnutrition-related diabetes, 32t
  - nutrient composition of diet, 58-59, 60t-61t
  - nutrition therapy, 53-54
  - protein intake, 58-59
  - recommendations for, 57-65, 60t-61t
  - saturated fats, 59, 60t
  - sucrose (sugar) intake, 62-63, 62t, 419
  - sweeteners, nutritive/nonnutritive, 63-64
  - vitamin, mineral, and herb supplements, 61t, 64
  - weights suggested for adults, 56t
- Obesity, 449-459. See also *Diet*; *Nutrition*; *Weight*.
- body mass index (BMI), 56t
  - central (visceral), 50t
    - metabolic syndrome and, 49, 50t
    - type 2 diabetes risk and, 25, 37, 41
  - fat intake, dietary, and, 59, 60t
  - insulin resistance and, 49, 449
  - insulin therapy in, 248-249, 278
- Obesity (*continued*)
- obese T2D patients vs lean patients, 72
  - pharmacologic treatment for, 449-459
    - liraglutide (Saxenda), 455-457
    - lorcaserin (Belviq), 451-453
    - naltrexone/bupropion (Contrave), 453-455
    - phentermine/topiramate (Qysmia), 449-451, 468-469
    - xenical (Orlistat), 462t, 465
  - prevalence of, 449
  - as risk factor for diabetes, 25, 37, 41
  - as risk factor for T2D, 25, 26, 37, 41
  - weight loss recommendations, 55-57, 61t
- Olestra, 64
- Omega-3 fatty acids, 59, 417
- in ORIGIN trial, 470t
- Onglyza. See *Saxagliptin (Onglyza)*.
- ONTARGET trial, 411
- Oral agents for type 2 diabetes, 83-90, 84t-89t. See also *specific agents and classes of agents*.
- in algorithm for treatment, 358
  - choice of, 84t-89t, 90
  - classes of agents, 83, 84t-89t
    - alpha-glucosidase inhibitors, 84t, 199-202
    - bile acid sequestrants (colesevelam), 84t, 217-221
    - dopamine receptor agonist (bromocriptine mesylate), 84t, 223-226
    - DPP-IV inhibitors, 84t-85t, 97-144
    - glinides, 85t, 209-215
    - metformin (biguanide), 84t, 91-95
    - SGLT2 inhibitors (canagliflozin), 86t, 145-180
    - sulfonylureas, 87t, 203-207
    - thiazolidinediones (TZDs), 87t, 181-198
  - combination agents, 85t-88t
    - DPP-IV inhibitor/biguanide, 85t, 94, 108-109
    - DPP-IV inhibitor/SGLT2 inhibitor, 85t, 126-127
    - DPP-IV inhibitor/TZD, 85t, 140-141
    - glinide/biguanide, 85t, 211
    - SGLT2 inhibitor/biguanide, 86t
    - sulfonylurea/biguanide, 87t, 94-95
    - thiazolidinedione/biguanide, 88t, 184, 186t-187t
    - thiazolidinedione/sulfonylurea, 88t, 184-185
  - combination therapy. See also *specific agents*.
  - contraindications, general, 90
  - dosage recommendations, 84t-89t
  - as initial pharmacologic therapy, 83
  - mechanisms of action, and treatment plan, 29
  - secondary failure of, 75, 76, 81
  - specific agents
    - acarbose, 84t, 199-200
    - alogliptin, 84t, 127-141
    - bromocriptine mesylate, 84t, 223-226
    - canagliflozin, 86t, 147-157
    - colesevelam, 84t, 217-221
    - dapagliflozin, 86t, 158-167
    - empagliflozin, 86t, 167-178
    - linagliptin, 85t, 119-126

- Oral agents for type 2 diabetes, specific agents (*continued*)
- metformin, 84t, 91-95
  - migliitol, 84t, 200-202
  - nateglinide, 85t, 212-214
  - pioglitazone, 87t, 182-192
  - repaglinide, 85t, 209-211
  - rosiglitazone, 87t, 181-182
  - saxagliptin, 85t, 109-118
  - sitagliptin, 85t, 98-108
  - sulfonylureas, 87t, 203-207
- Oral glucose tolerance test (OGTT), 28, 36, 44, 358
- ORIGIN trial, 268, 468, 470t
- Orinase. See *Tolbutamide*.
- Orlistat. See *Xenical*.
- Orthostatic hypotension, 411, 440
- Oseni (alogliptin/pioglitazone), 85t, 140-141
- Pacific Islanders, 15, 17, 41
- Pancreatic disease, diabetes secondary to, 32t
- Pancreatic insulin secretion. See *Insulin secretion*.
- Pancreatitis
- diabetic ketoacidosis and, 386t
  - dulaglutide and, 328-329
  - lixisenatide and, 331
- Pathophysiology of type 2 diabetes, 23-27
- etiologic sequence, 23-27
  - genetic component, 23, 34-35
  - heterogeneity in, 23-25, 227-228
  - metabolic abnormalities, 23-25, 24, 26, 27-28, 27, 72
  - interrelationship of, 28
  - natural history of diabetes, 27-29, 27
  - pharmacologic therapy, basis for, 72-73
  - physiologic processes in, 26
  - transition from prediabetes, 23-28, 27
- Patient education, 28
- about diabetic ketoacidosis, 393
  - about diabetic retinopathy, 426
  - about hypoglycemia, 399-400
  - about insulin therapy, 237
  - and backups for interruption of, 393
  - about self-monitoring of blood glucose (SMBG), 237, 368
  - with Diabetes Warranty Program, 45, 46-47
- Patient motivation, 366, 368
- PCSK-9 inhibitors, 417, 421-423, 421t
- PDE-5 inhibitors, 442-444, 443t
- Peripheral occlusive disease, 410
- Peripheral vascular disease, 405
- PGC. See *Plasma glucose concentration*.
- Pharmacologic therapy for type 2 diabetes, 71-82. See also *Oral agents for type 2 diabetes; Treatment of type 2 diabetes; and specific agents*.
- as adjunct to diet and exercise, 71, 83
  - aggressive management, 71
  - algorithm for treatment, 355-360, 358-359
- Pharmacologic therapy for type 2 diabetes (*continued*)
- glucoregulatory hormones, 283-354
  - amylin analogue (pramlintide), 343-350
  - GLP-1 analogues, 286-342
  - incretins, 283-286
  - hyperglycemia, importance of controlling, 73-74, 74t
  - insulin therapy, 227-282
  - intensive therapy, 74-80
  - oral agents, 83-90, 84t-89t
    - secondary failure of, 75, 76, 81
  - overview of, 71-90
  - pathophysiologic basis of, 72-73
  - triple oral/injectable therapy, 358
- Phenotype B pattern, 413
- Phentermine/topiramate (Qysmia), 449-451
- CONQUER and SEQUEL trials, 468-469, 470t
- prescribing information, 450-451
- D-phenylalanine derivative. See *Nateglinide*.
- Phosphate replacement, 388, 392, 396
- Phosphodiesterase-5 (PDE-5) inhibitors, 442-444, 443t
- Physical activity. See *Exercise; Sedentary lifestyle*.
- Pioglitazone (Actos), 87t, 182-192, 469
- combination formulations, 88t, 184-185, 196
  - with DDP-4 inhibitor-alogliptin (Oseni), 85t, 140-141
  - with metformin (Actoplus Met/Actoplus Met XR), 88t, 184, 186t-187t
  - with SFU-glimepiride (Duetact/Avandaryl), 88t, 184-185
- combination therapy, 182-188
- with alogliptin, 131, 133t, 134t-135t, 136-137
  - with empagliflozin, 168, 170t
  - with linagliptin, 123
  - with lixisenatide, 331
  - with metformin, 136-137, 182, 184
  - with sitagliptin, 101, 103
- dosage, 87t, 190-192
- effects/benefits of
- cardiovascular risk, 185-188, 188
  - glycemic control, 182, 184-185, 186t-187t, 191
  - lipid levels, 185
- prescribing considerations, 190
- Actoplus Met, 190-191
  - Duetact, 191-192
- side effects, 192-196
- CHF and edema, 193-194, 194t
  - liver toxicity, 192-193
- trials and studies
- ACT-NOW, 462t, 466-467, 467
  - combination therapy, 182-188
  - IRIS, 469, 470t
  - monotherapy, 182, 183
  - PROactive Study, 188-190, 190, 191, 195
- Plasma glucose concentration (PGC), 42-43, 361-363
- as diagnostic criteria, 42-43, 43t
  - factors influencing, 28f
  - normal values, 42t
  - postprandial, 73-74, 74t

- Plasma glucose concentration (PGC) (*continued*)  
 target/goal values, 356t, 406  
 testing for, 28, 42-44, 43t, 361-363  
   home monitoring. See *Self-monitoring of blood glucose*.  
   limitations of, 263  
   timing of measurements, 363
- Polycystic ovary syndrome, 42
- Polydipsia, 41, 385, 387, 394
- Polyphagia, 41, 387
- Polyunsaturated fats, 419
- Polyuria, 41, 385, 387
- Postprandial glucose (PPG), 73-74, 363. See also *Hyperglycemia, postprandial*.  
 amylin/pramlintide and, 343, 344-345  
 gastric emptying and, 343  
 importance of controlling, 73-74  
 nateglinide and, 212-213, 214  
 target levels, 74t, 356t, 362t
- Postprandial hyperglycemia. See *Hyperglycemia, postprandial*.
- Potassium  
 dietary, 64, 407  
 monitoring, 410  
 replacement therapy, 388, 391-392, 396
- PPG. See *Postprandial glucose*.
- Pramlintide (Symlin), 343-350. See also *Amylin*.  
 action mechanisms, 343  
 adverse events, 348-349  
 dosing, 349-350  
 efficacy, 343-347  
   clinical practice study (assessment), 346-347, 347  
   long-term glycemic control, 345-346, 346  
   postprandial glucose, 343-345  
 gastric emptying and, 343  
 hypoglycemia and, 348-349  
 practical tips for patient, 349-350  
 tolerability, 348  
 weight loss effects, 345, 346, 346, 347-348
- Prandimet (repaglinide/metformin), 85t, 211
- Prandin. See *Repaglinide*.
- Precose. See *Acarbose*.
- Prediabetes, 25, 27-28, 27, 36-37, 37t. See also *Impaired glucose tolerance (IGT)*.  
 diagnostic criteria, 36-37, 37t, 43t  
 prevalence of, 461  
 screening for, 28, 470-472  
 transition to T2D, 23-28, 27, 36-37, 472  
   continuum in, 27, 27  
   T2D treatment and, 91  
 treating, 461-475  
 undiagnosed, 461  
 vs T2D, 27
- Pregnancy, 90. See also *Gestational diabetes mellitus*.
- Prevalence  
 of prediabetes, 461  
 of type 2 diabetes, 15-18, 16, 17
- Prevention of type 2 diabetes, 461-475. See also *Early detection and management; Primary prevention trials*.  
 clinical trials  
   primary prevention trials, 461-468, 462t  
   reduced diabetes risk in other trials, 468-470, 470t  
 intensive glycemic control, 74-80  
 intensive therapy, 74-80, 237-238, 249  
 need for/importance of, 20, 472  
 screening and, 470-472  
 summary, 472
- Primary prevention trials, 461-468, 462t  
 ACT-NOW, 462t, 466-467, 467  
 Da Qing (IGT and Diabetes Study), 461-462, 462t  
 DPP (Diabetes Prevention Program), 462t, 463-464  
 DREAM, 462t, 465-466  
 FDPS (Finnish Diabetes Prevention Study), 462-463, 462t  
 Indian DPP, 462t  
 NAVIGATOR, 468  
 STOP-NIDDM, 462t, 465  
 TRIPOD, 462t, 464-465  
 XENDOS, 462t, 465
- PROactive Study, 188-190, 190, 191, 195
- Protein, 58-59, 436. See also *Diet; Nutrition*.
- Proteinuria, 410
- Pump therapy (insulin), 236t, 249-251, 358
- Quality of life, impact of diabetes on, 383, 400
- Qysmia (phentermine/topiramate), 449-451, 468-469
- Race/ethnicity  
 abdominal obesity criteria and, 51  
 incidence of diabetes and, 17  
 prevalence of T2D and, 15, 17, 18, 228  
 risk for diabetes and, 26, 37, 38, 41
- Ramipril, 410  
 in DREAM trial, 462t, 465-466  
 in HOPE trial, 470t
- Ranibizumab, 430
- RECORD trial, 195-196
- Renal disease  
 antihypertensive agents, potential benefits of, 410t  
 blood pressure and, 432-433  
 lixisenatide and, 331  
 nephrotoxic drugs, 431  
 sitagliptin and, 106-107
- Renal function. See also *Diabetic nephropathy*.  
 ACE inhibitors and, 408, 410, 410t  
 renal insufficiency, factors influencing, 431-432
- Repaglinide (Prandin), 85t, 209-211  
 action mechanism, 209  
 combination therapy, 210  
   fixed-dose combination with metformin (PrandiMet), 85t, 211  
   with metformin, 209-210, 210  
   triple-combination (TZD/repaglinide/MET), 210  
 contraindications, 209



- Repaglinide (Prandin) (*continued*)  
 dosage, 85t  
 glycemic control with, 209-210, 210  
 monotherapy, 209-210  
 prescribing information, 211  
 side effects, 211
- Resources on diabetes, 477-484
- RESTORE trial, 430
- Retinopathy. *See Diabetic retinopathy.*
- Risk factors, cardiovascular. *See Cardiovascular risk.*
- Risk factors for diabetes, 15, 19, 26-27, 41-42  
 gestational diabetes mellitus as, 35  
 reduction or prevention, clinical trials on, 461-475, 462t
- Risk of death from diabetes, 19-20
- Rosiglitazone (Avandia), 87t, 181-182  
 combination formulations (Avandamet; Avandaryl), 88t, 181  
 dosage, 87t  
 safety concerns, 182, 194-196  
 trials and studies  
   DREAM trial, 29, 462t, 465-466  
   with liraglutide, 303-304, 305, 306-308, 307
- Ryzodeg (degludec + aspart injection), 229, 244, 245  
 efficacy, 276-277  
 premixed 70/30, 249, 275, 276-278  
 safety, 277-278  
 starting or switching to, 277  
 time course of action, 233t
- Salt, dietary intake of, 60t, 419
- Saturated fats, 59, 60t
- SAVOR-TIMI 53, 116, 138
- Saxagliptin (Onglyza), 85t, 109-118  
 adverse events, 117  
 cardiovascular outcomes, 116  
 combination agent with metformin XR (Kombiglyze XR), 85t, 118  
 combination therapy, 110-114  
   with glyburide, 112-114  
   with metformin, 110-112, 111, 114  
   with TZDs, 114, 115  
 dosage, 85t, 117-118  
 efficacy, 109-116  
 indications for, 109  
 prescribing considerations, 117-118  
 renal impairment and, 117  
 trials and studies, combination, 110-114
- Saxenda (liraglutide), 455-457
- Screening  
 for ankle-brachial index (ABI), 445  
 for diabetes, 28, 470-472  
 for dyslipidemia, 414  
 for gestational diabetes (GDM), 35-36, 44  
 for prediabetes, 28, 470-472
- Secondary diabetes, 32t-33t
- Sedentary lifestyle, 19, 25, 27, 37, 42, 406
- Self-monitoring of blood glucose (SMBG), 366-373  
 advances in, 373-380  
 advantages and disadvantages of, 368-369  
 in assessment of glycemic control, 262-263  
 blood glucose meters, 369  
 bloodletting, 373-379  
 continuous glucose monitoring systems, 379-380  
 dietary adjustments and, 54, 62, 370-371  
 errors in, 369  
 exercise and, 69t  
 frequency of, 367, 369-370  
 hypo- and hyperglycemia prevention with, 279, 367, 399  
 logbook, 372, 374-375  
 patient dosage adjustment via, 204, 241, 242t, 249, 362, 372-373, 372t  
   algorithm form, 376-377  
   split-mixed regimen, 373, 378t  
   techniques for premeal hyperglycemia, 372t  
 patient education on, 237, 368  
 patient motivation for, 366  
 for patients not taking insulin, 370-371  
 for patients taking insulin, 371-372  
 reasons for performing, 367-368, 371  
 recommendation for ALL diabetes patients, 369-370  
 systems for, 369  
 time of day for measurements, 371  
   at peak time of insulin action, 232t-234t  
   who should perform, 369-370
- Semmes Weinstein (SW) monofilaments, 444-445
- SEQUEL trial, 468-469, 470t
- SFUs. *See Sulfonylureas.*
- SGLT2 inhibitors. *See Sodium-glucose transporter 2 (SGLT2) inhibitors.*
- Sildenafil (Viagra), 442, 443t
- Sitagliptin (Januvia), 85t, 98-108  
 adverse events, 107  
 cardiovascular outcomes, 105-106  
 in combination or add-on therapy, 98, 100-105  
   with glimepiride, 104  
   with glipizide, 101-104  
   with insulin, 104-105  
   with metformin, 100-101, 102  
     fixed-dose formulation (Janumet; Janumet XR), 85t, 108-109  
   with pioglitazone, 101, 103  
 dosing, 85t, 107-108  
   for Janumet, 85t, 108-109  
   for Janumet XR, 85t, 109  
 efficacy, 98-105  
   compared with MET, 99-100  
   long-term efficacy, 100  
 hypoglycemia and, 107  
 indications for, 98  
 prescribing considerations, 107-108  
 renal disease patients and, 106-107  
 trials and studies  
   combination or add-on therapy, 100-105  
   monotherapy, 98-100, 105

- Sitagliptin/metformin (Janumet), 85t, 108-109  
 Sleep disturbances, 383, 454-455  
 SMBG. See *Self-monitoring of blood glucose*.  
 Smoking, 48, 406, 455  
 Sodium, dietary intake of, 60t, 407, 419  
 Sodium-glucose transporter 2 (SGLT2) inhibitors, 86t, 145-180. See also *specific agents*.  
   action mechanism, 145, 146  
   actions, 408, 435  
   agents  
     canagliflozin (Invokana), 86t, 147-157  
     dapagliflozin (Farxiga), 86t, 158-167  
     empagliflozin (Jardiance), 86t, 167-178  
   in algorithm for treatment, 358  
   combination agents  
     with biguanide (metformin), 86t  
     with DPP-IV inhibitor (empagliflozin/linagliptin), 85t, 126-127, 128  
 Soliqua 100/33 (insulin glargine/lixisenatide), 340-342  
 SPRINT trial, 407  
 Starlix. See *Nateglinide*.  
 Statins, 51, 417, 420-421, 421t, 422t  
   trials involving, 469, 470t  
 Statistics on Type 2 diabetes, 15-22  
 Stendra (avanafil), 442, 443t  
 Steno-2 Trial, 77, 78, 405  
 STOP-NIDDM study, 29, 462t, 465  
 Stroke, 410t, 469  
 Subtilisin/kexin type 9 inhibitors. See *PCSK-9 inhibitors*.  
 Sugar (sucrose) intake, 61t, 62-63, 419  
 Sugar alcohols, 63  
 Sulfonylureas, 87t, 203-207. See also *specific drugs*.  
   action mechanism, 203  
   in algorithm for treatment, 358  
   combination agents  
     sulfonylurea/biguanide agents, 87t, 94-95  
     thiazolidinedione/sulfonylurea agents, 88t  
   combination therapy  
     with exenatide, 287, 288t  
     with liraglutide, 121-122, 299  
     with lixisenatide, 331  
     with metformin, 94-95  
     with pioglitazone (Duetact), 88t, 184-185  
     with sitagliptin, 98  
   dosage, 87t, 204  
   of combination agents, 87t, 88t  
   efficacy, 203  
   first generation, 87t, 203  
     acetohexamide (Dymelor), 87t, 203  
     chlorpropamide (Diabinese), 87t, 203  
     tolazamide (Tolinase), 87t, 203  
     tolbutamide (Orinase), 87t, 203  
   hypoglycemia and, 204, 205  
   prescribing information, 204-205  
   second generation, 87t, 203, 205-206  
     glimepiride (Amaryl), 87t, 203, 205-206  
     Sulfonylureas, second generation (*continued*)  
       glipizide (Glucotrol), 87t, 203, 206  
       glipizide, extended release (Glucotrol XL), 87t, 203, 206  
       glyburide (DiaBeta, Micronase, Glynase PresTab), 87t, 203, 206  
       side effects, 204  
       in UKPDS, 75-77  
       weight gain and, 205  
   Supplements, dietary, 62t, 64  
   Sweeteners, nutritive/nonnutritive, 63-64  
   Symlin. See *Pramlintide*.  
   Symptoms of diabetes/type 2 diabetes, 41  
   Synjardy, Synjardy XR (empagliflozin/metformin), 86t  
  
 Tadalafil (Cialis), 442, 443t  
 Taking Control of Your Diabetes (TCOYD), 484  
 Tandem t:flex insulin pump, 252-255  
 Tanzeum. See *Albiglutide*.  
 TECOS study, 105-106  
 Testosterone, 442  
 T:flex insulin pump, 252-255  
 Thiazide diuretics, 409t, 410t, 412  
 Thiazolidinediones (TZDs), 87t, 181-198. See also *Pioglitazone*; *Rosiglitazone*  
   action mechanisms, 181  
   agents  
     pioglitazone (Actos), 87t, 182-192  
     rosiglitazone (Avandia), 87t, 181-182  
   in algorithm for treatment, 358  
   cardiovascular risk and, 181, 193-196  
   cautions, warnings, and contraindications, 192-196  
   combination agents, 184-185, 196  
     with biguanide, 88t, 184, 186t-187t  
     with DPP-4 inhibitor, 85t, 140-141  
     with sulfonylureas, 88t, 184-185  
   triple-combination (TZD/repaglinide/MET), 210  
   combination therapy  
     with exenatide, 287, 289  
     with liraglutide, 299  
     with metformin, 94  
     with saxagliptin, 114, 115  
     with sitagliptin, 98  
   dosage, 87t  
   as first-line therapy, 29  
   in prevention of diabetes, 51, 469, 470t  
   side effects, 192-196  
     CHF and edema, 193-194, 194t  
     CVD and mortality risk, 194-196  
     liver toxicity, 192-193  
   summary, 196  
   Thrifty gene hypothesis, 18-19  
   Tolazamide (Tolinase), 87t, 203  
   Tolbutamide (Orinase), 87t, 203  
   Tolinase (tolazamide). See *Tolazamide*.  
   Toujeo (glargine U-300), 229, 245, 270-271, 272t  
   time course of action, 233t, 235  
   Tradjenta. See *Linagliptin*.

- Transcutaneous nerve stimulation (TENS), 438
- Treatment of type 2 diabetes. See also *Oral agents for type 2 diabetes; and specific agents and classes of agents.*
- algorithm for, 355-360, 358-359
    - differences in consensus algorithms, 357-360
  - assessment of treatment, 361-382. See also *Assessment of treatment regime.*
  - cost effectiveness of, 471
  - diet and nutrition in, 53-66, 355, 357, 406
  - disease progression and, 238, 239, 246
  - early. See *Early detection and management.*
  - glycemic control with
    - importance of, 73-74, 74t, 357, 366, 379, 405-406, 426
    - intensive therapy for, 74-80, 237-238
    - target levels/goals, 74t, 80, 356t, 357, 406
  - goals of, 355-357, 366, 406
    - metabolic goals, 49, 362t
  - hyperglycemia, importance of controlling, 73-74, 74t
  - individualized approach in, 355-357
  - intensive therapy, 74-80, 237-238
    - benefits of, 20, 74, 75-78, 75t
    - reduced complications with, 74-77, 75t
  - in lean vs obese patients, 72
  - nonpharmacologic, 53-69
    - exercise, 67-69, 357, 406
    - nutrition, 53-66, 406
    - pharmacologic concurrent with, 71, 83
  - pharmacologic
    - glucoregulatory hormones, 283-354
    - insulin therapy, 227-282
    - oral agents, 83-226, 84t-89t
    - overview, 71-90
    - pathophysiologic basis of, 72-73
    - secondary failure of, 75, 76, 81
    - therapeutic plan, development of, 28-29
- Tresiba. See *Degludec U-100 and U-200 (Tresiba).*
- Triglycerides, 413, 414t, 415
  - high, cardiovascular risk and, 48
  - hypertriglyceridemia, 413, 414t
    - severe, 421
    - treatment for, 421, 422t, 423
  - lowering, 421t
  - target/goal levels, 362t, 417t, 418, 419, 421
- TRIPOD study, 462t, 464-465
- Troglitazone, 462t, 463-465
- Trulicity. See *Dulaglutide.*
- Twin studies, 23, 34-35
- Type 1 diabetes (T1D), 31-34, 32t. See also *Diabetes mellitus.*
- age of onset, 34
  - diabetic ketoacidosis in, 387
  - differences from type 2 diabetes, 35, 38, 245
  - in elderly, 385
  - hypoglycemia and, 279
  - therapy for, 34, 249
- Type 2 diabetes (T2D), 32t, 34-35. See also *Diabetes mellitus; Treatment of type 2 diabetes.*
- age of onset, 35
  - aging process and, 25-26, 27
  - algorithm for treatment, 355-360, 358-359
  - assessment of treatment regime, 361-382
  - asymptomatic, 16-18, 41
  - classification of, 31-39, 32t-33t
    - problems with, 38
  - complications of, 383-448
  - continuum of, 27, 27
  - differences from type 1 diabetes, 35, 38, 245
  - heterogeneous nature of, 23-25
  - incidence, 15, 16-18, 16, 20, 21
  - metabolic abnormalities in, 23-25, 24, 27-28, 27, 72
  - natural history of, 27-29, 27, 75, 227, 471
  - pathophysiology, 23-27
  - pharmacologic treatment, overview, 71-90
  - prevalence, 15-18, 16, 17
  - prevention of, 461-475
  - resources, 477-484
  - signs and symptoms of, 27, 41
  - statistics on, 15-22
  - transition from prediabetes to, 23-28, 27, 36-37
  - undiagnosed, 16-18, 394, 461
- TZDs. See *Thiazolidinediones.*
- U-100
  - Basaglar U-100 (insulin glargine follow-on biologic), 269-270
  - Humalog (lispro) U-100, 228, 257
  - Humulin R U-100, 264
  - Lantus (glargine) U-100, 229, 266-269
  - Tresiba (degludec) U-100, 229, 233t, 245, 271-275
- U-200
  - Humalog (lispro) U-200, 228, 257
  - Tresiba (degludec) U-200, 229, 233t, 245, 271-275
- U-300, Toujeo (glargine) U-300, 229, 245, 270-271, 272t
- U-500 (Humulin R U-500), 264-266, 270
- UKPDS (United Kingdom Prospective Diabetes Study), 18, 74-77
  - antihypertensive agents, 408, 411
  - cardiovascular risk reduction in, 75-77, 75t, 91
  - dyslipidemia in, 413
  - glycemic control benefits, 74-75, 75t, 76, 367
  - secondary failure in, 75, 76
  - weight gain on, 278
- Undiagnosed diabetes, 16-18, 394, 461
- United Kingdom Prospective Diabetes Study. See *UKPDS.*
- Urinary tract infections, 400, 403t, 433
- V-Go Insulin Delivery Device, 251-252, 251, 253, 254, 255t, 256
- VA-NEPHRON D trials, 411
- VADT (Veterans Affairs Diabetes Trial), 78-79, 80
- VALUE trial (valsartan), 470t
- Vardenafil (Levitra), 442, 443t
- Vascular disease, as risk factor for diabetes, 42. See also *Macrovascular disease.*

- Verapamil, 411-412
- Veterans Affairs Diabetes Trial (VADT), 78-79, 80
- Viagra (sildenafil), 442, 443t
- Victoza. See *Liraglutide*.
- Vision. See *Diabetic retinopathy; Eyes*.
- Vitamins/vitamin supplements, 61t, 64
- Vulvovaginitis, 402t
  
- Warranty Program, Diabetes, 45, 46-47
- Weight, 55-57, 56t, 355, 357, 406. See also *Obesity*.
  - gain
    - with insulin therapy, 278-279
    - with sulfonylureas, 205
  - goal levels, 55-57, 56t, 362t
  - ideal/suggested, 55-57, 56t
  - loss or neutrality, 55-57, 61t, 357, 449, 457
    - albiglutide and, 319-320
    - benefits of, 55
    - caloric intake for, 55, 57-58
    - canagliflozin and, 152, 155
    - dapagliflozin and, 158, 165
    - empagliflozin, 168, 174
    - exenatide and, 291, 291, 292-293, 292, 294, 295, 296
    - exercise and, 55
    - GLP-1 therapy and, 337
    - pharmacologic treatments for, 449-459
    - pramlintide and, 345, 346, 346, 347-348
    - Soliqua 100/33, 341-342
    - strategies for, 55-57
    - weight categories, 56t
- Welchol. See *Colesevelam*.
- WOSCOPS study, 470t
  
- XENDOS trial, 29, 462t, 465
- Xenical (in XENDOS trial), 29, 462t, 465
- Xigduo XR (dapagliflozin/metformin), 86t
- Xultophy 100/3.6 (insulin degludec/liraglutide), 338-340
  
- Yeast infections, 41