Drug Class / Category	Mechanism	Drugs / Subtypes	Effects	Side Effects	Interactions / Contraindications / Notes (FULL INFO)
DIURETICS	Modulate electrolyte transport at nephron → ↓ plasma volume → ↓ CO	Carbonic anhydrase inhibitors; Loop diuretics; Thiazides; K^+-sparing diuretics	↓ BP, ↓ volume; highly effective in low-renin HTN; highly effective in African Americans	↑ Lipids, ↓ insulin sensitivity; initial ↑ PVR; take 2 weeks for full BP effect	Reduced efficacy in renal failure due to transporter dysfunction; may fail when kidney is damaged
NEPHRON SITES AFFECTED	Site-specific natriuresis	PCT (65–70%), TAL (25%), DCT (5%), Collecting duct (1–2%)	Determines diuretic intensity	—	History: Discovered 1930s (antibacterial side effect); applied to hypertension in 1950s by Schwartz & Beyer
CALCIUM CHANNEL BLOCKERS (CCBs) – DHPs	Block Ca^{2+} entry into vascular smooth muscle → vasodilation	Amlodipine, Nifedipine	↓ PVR → ↓ BP	Hypotension, reflex tachycardia, headache, flushing, edema	Amlodipine + ACEI ↓ CV events (ASCOT trial); preferred in low-renin HTN, elderly, isolated systolic HTN
CALCIUM CHANNEL BLOCKERS (CCBs) – Non-DHPs	Block Ca^{2+} channels in heart → ↓ HR, ↓ AV conduction, ↓ contractility	Verapamil, Diltiazem	Negative inotrope, negative chronotrope; ↓ BP	Cardiac depression	Additive AV block with β-blockers; ↑ digoxin toxicity; avoid in LV dysfunction
β-BLOCKERS — Heart Effects	Block β_1 → ↓ cAMP → ↓ PKA → ↓ Ca^{2+} influx → ↓ HR, ↓ contractility	Propranolol (NS), Atenolol (β_1), Metoprolol (β_1), Nadolol (NS)	↓ CO; ↓ AV conduction; block reflex tachycardia	Bradycardia, AV block, bronchospasm, nightmares, depression, ↑ TG, ↓ HDL, glucose intolerance	Contra: asthma, PVD, AV block; lipid-soluble forms cross BBB → nightmares; combine with vasodilators to prevent tachycardia; useful in HF, MI, ischemia
β-BLOCKERS — Vascular Effects	β_2 normally causes vasodilation (↑ cAMP); blocking β_2 → mild ↑ PVR	—	Mild vasoconstriction initially	—	Short-term ↑ PVR only; long-term ↓ BP via renin suppression
β-BLOCKERS — Kidney Effects	Block β_1 receptors in JG cells → ↓ renin → ↓ Ang II → ↓ aldosterone	—	↓ Na^+ retention; ↓ vasoconstriction	—	Extremely effective in high-renin hypertension (common in young patients)
ACE INHIBITORS	Block conversion of Ang I → Ang II; prevent bradykinin breakdown → vasodilation	Enalapril, Ramipril, Lisinopril, Captopril	↓ PVR, ↓ aldosterone, ↓ Na^+ retention; renoprotective in diabetics	Cough (10–20%), hyperkalemia, angioedema (0.1–0.5%), rash, taste changes, severe hypotension in hypovolemia	Contra: pregnancy (2nd/3rd trimester), renal artery stenosis; avoid with K^+-sparing diuretics; possibly less effective in African Americans; dose adjust in renal impairment
ARBs	Block AT_1 receptor → ↓ TPR, ↓	Losartan	↓ Vasoconstriction; ↓ sympathetic	Angioedema, dizziness	Contra: pregnancy; AT_2 activity remains → vasodilation, NO/PGI_2 release, natriuresis; ACEI

	aldosterone, ↓ Na^+ retention		tone; ↓ water/Na^+ retention		cheaper—ARBs used when ACEI not tolerated (cough/angioedema)
AT_1 RECEPTOR EFFECTS BLOCKED BY ARBs	Prevent vasoconstriction, aldosterone release, sympathetic activation, Na^+/water retention, cell growth	—	—	—	AT_2 stimulation remains → ↑ NO, ↑ PGI_2, vasodilation, natriuresis, anti-proliferation
PERIPHERAL α_1 BLOCKERS	Block NE binding to vascular α_1 receptors → vasodilation	Prazosin, Doxazosin, Terazosin	↓ PVR, ↓ BP	First-dose syncope, postural dizziness, headache, drowsiness	NOT first-line (ALLHAT: ↑ heart failure risk); used as add-on therapy; helpful in BPH (Doxazosin, Terazosin)
ADRENERGIC NEURON BLOCKERS	Deplete NE from sympathetic nerve terminals; inhibit NE release	Guanethidine, Reserpine	↓ CO, ↓ PVR	Orthostatic hypotension, depression, bradycardia, impotence, diarrhea, Na^+/H_2O retention	Rarely used; TCAs, MAOIs, amphetamines block uptake → reverse effect; reserpine is cost-effective but causes severe depression
CENTRAL α_2 AGONISTS	Stimulate CNS α_2 → ↓ sympathetic outflow → ↓ HR, ↓ CO, ↓ PVR, ↓ renin	Clonidine, Methyldopa, Guanabenz, Guanfacine	↓ BP via central inhibition	Dry mouth (44%), sedation (50%), dizziness (15%), methyldopa → hemolytic anemia	Methyldopa = first-choice in pregnancy; TCAs block antihypertensive effect; barbiturates reduce efficacy; MAOI + clonidine → HTN crisis; clonidine patch available (weekly)
GANGLIONIC BLOCKERS	Block transmission in sympathetic & parasympathetic ganglia	Trimethaphan, Pentolinium, Mecamylamine	**Immediate and profound ↓ BP**	Numerous severe systemic side effects	Only used for controlled hypotension intraoperatively or hypertensive crisis; potentiate tubocurarine; histamine release (caution in allergies)

VASODILATOR – Hydralazine	Directly relaxes arteriolar smooth muscle (↓ Ca^{2+}, hyperpolarization)	Hydralazine	↓ PVR	Reflex tachycardia (dangerous in elderly or CAD), Na^+/H_2O retention, headache, nausea, lupus-like syndrome	Effect lasts 12 h despite 1 h t½ (arterial wall storage); combine with β-blocker + diuretic
VASODILATOR – Minoxidil	Opens KATP channels → strong hyperpolarization → arteriolar dilation	Minoxidil	Large ↓ PVR	Hypertrichosis (excess hair growth), edema, reflex tachycardia	Reserved for severe refractory HTN; must be combined with diuretic + β-blocker; effect lasts 12–24 h
VASODILATOR – Fenoldopam	D_1 receptor agonist → vasodilation + natriuresis + renal vasodilation	Fenoldopam	↓ BP; improves renal blood flow	—	IV, short-acting; used in emergency or postoperative HTN
VASODILATOR – Sodium Nitroprusside (SNP)	Releases NO → rapid vasodilation of arteries & veins	SNP	Immediate ↓ PVR	Cyanide accumulation → lactic acidosis; rebound HTN; tolerance	IV only; light-sensitive; effect ends when infusion stops; used for hypertensive emergencies
VASODILATOR – Diazoxide	Opens KATP channels → arteriolar dilation	Diazoxide	↓ BP	Tachycardia, angina	IV; onset 2 min; duration 6–24 h; used in hypertensive emergencies
VASODILATOR – Labetalol / Carvedilol	Combined α_1 + β blockade → vasodilation **without reflex tachycardia**	Labetalol, Carvedilol	Rapid ↓ BP	Minimal	Oral/IV; used in hypertensive crisis & pheochromocytoma; Labetalol α:β = 1:3, Carvedilol α:β = 1:10
COMPENSATORY RESPONSES TO VASODILATORS	Vasodilators ↓ PVR → triggers ↑ sympathetic tone & ↑ renin	—	↑ HR, ↑ contractility, ↑ aldosterone, Na^+/H_2O retention	—	Managed using **diuretics + β-blockers**

Lipid lowering agents

Drug Class / Category	Mechanism of Action (FULL DETAILS)	Drugs / Subtypes	Effects on Lipids & Atherosclerosis	Side Effects / Toxicity	Interactions / Contraindications / Clinical Notes (COMPLETE)
STATINS (HMG-CoA Reductase Inhibitors)	Competitive inhibition of HMG-CoA reductase → ↓ mevalonate → ↓ hepatic cholesterol synthesis → ↑ LDL receptor expression → ↑ LDL clearance. Also "pleiotropic effects": improved endothelial function, ↓ vascular inflammation, ↓ platelet aggregation, antithrombotic, plaque stabilization, ↑ neovascularization of ischemic tissue, enhanced fibrinolysis, immune suppression, ↑ osteoblast activity, osteoclast apoptosis.	Simvastatin (prodrug), Mevastatin, Lovastatin, Pravastatin, Fluvastatin, Atorvastatin, Rosuvastatin	↓ LDL (30–50%); ↓ total cholesterol; mild ↓ TG; mild ↑ HDL; ↓ morbidity/mortality in CAD; ↓ MI & stroke (primary & secondary prevention).	Mild GI upset, ↑ liver enzymes, **myositis / rhabdomyolysis** (risk ↑ with fibrates or niacin), angioedema (rare).	Contra: **pregnancy**, active liver disease. PK: orally absorbed; strong first-pass hepatic extraction (target organ is liver). Simvastatin = inactive prodrug. Atorvastatin effective in homozygous familial hypercholesterolemia. Monitor CK & LFTs.
NIACIN (Vitamin B3)	Inhibits adipocyte adenylyl cyclase → ↓ lipolysis → ↓ FFA transport to liver → ↓ hepatic TG synthesis. Also inhibits diacylglycerol acyltransferase-2 → ↓ VLDL synthesis → ↓ LDL. Increases HDL by ↓ hepatic uptake of ApoA-I. ↓ fibrinogen; ↑ plasminogen activator.	Nicotinic Acid (Vitamin B3)	**BEST drug to ↑ HDL (35–40%)**; ↓ TG (35–45%); ↓ LDL (20–30%); ↓ VLDL; improves fibrinolysis.	Cutaneous flushing/warmth, pruritus, rash, dry skin, **acanthosis nigricans**, nausea, vomiting, diarrhea, **hepatotoxicity**, hyperuricemia (gout), hyperglycemia/insulin resistance, arrhythmias, visual disturbances.	Avoid in liver disease, gout, severe peptic disease. Completely absorbed; peaks in 1 hr; short half-life → 2–3 doses/day. Flushing reduced with aspirin.
FIBRATES (PPAR-α Activators)	Activate PPAR-α → ↑ β-oxidation of fatty acids, ↑ LPL expression → ↑ lipolysis of TG-rich lipoproteins; ↓ ApoC-III (LPL	Clofibrate, Gemfibrozil, Fenofibrate, Bezafibrate	**↓ TG (40–60%)**; ↓ VLDL; ↓ LDL (variable); ↑ HDL (modest). **DRUG OF CHOICE for severe hypertriglyceridemia.**	Rash, urticaria, hair loss, GI upset, impotence, anemia, **myopathy**, rhabdomyolysis, fatigue, gallstones	**Statin + fibrate = 10× ↑ risk of rhabdomyolysis** (esp. gemfibrozil). Avoid in renal failure. Improve insulin resistance.

	inhibitor); ↑ ApoA-I & ApoA-II → ↑ HDL.			(cholesterol), ↑ transaminases.	
BILE ACID–BINDING RESINS	Large anionic polymers bind bile acids in intestinal lumen → prevent reabsorption → ↑ bile acid synthesis from cholesterol → ↓ hepatic cholesterol → ↑ LDL receptor expression → ↑ LDL clearance.	Colestipol, Cholestyramine, Colesevelam	↓ LDL significantly; modest ↑ HDL; **may ↑ TG**	Constipation, bloating, unpleasant taste, GI distress	Interfere with absorption of drugs (warfarin, digoxin) & fat-soluble vitamins. Safe in pregnancy. Increase cholesterol synthesis via upregulated HMG-CoA reductase (partially offsets effect).
EZETIMIBE (Sterol Absorption Inhibitor)	Inhibits NPC1L1 transporter in jejunal enterocytes → ↓ intestinal cholesterol absorption by **54%** → ↓ chylomicron cholesterol → ↓ delivery to liver → ↑ LDL receptor expression → ↑ LDL clearance.	Ezetimibe	↓ LDL (15–20%); **synergistic with statins** (up to 60% LDL reduction).	Allergic reactions, reversible ↑ LFTs, **myopathy** (rare).	Does NOT affect TG absorption. Causes compensatory ↑ cholesterol synthesis (blocked if combined with statin). Excellent add-on therapy.

DRUG TREATMENT OF ISCHEMIC HEART DISEASE

Category / Drug Class	Mechanism (FULL DETAILS)	Drugs / Subtypes	Effects on Angina / Myocardium	Side Effects / Toxicity	Notes / Interactions / Clinical Use (ALL DETAILS)
Stable Angina	Atherosclerotic narrowing → ↓ coronary perfusion during exertion → O_2 demand > supply.	—	Relieved rapidly by rest or nitroglycerin.	—	Most common form; predictable pattern.
Unstable Angina	Combination of thrombosis, plaque rupture, vasospasm → unpredictable ischemia.	—	More severe; occurs at rest.	—	Requires aggressive therapy (HTN, lipids). Precursor to MI.
Variant (Prinzmetal) Angina	Coronary artery spasm (smooth muscle contraction).	—	Responds rapidly to nitrates & CCBs.	—	Occurs at rest, unrelated to exercise.
IHD Mechanism (Global Concept)	Ischemia = **O_2 supply / O_2 demand imbalance**. Coronary flow ↓ or myocardial work ↑.	—	—	—	Key treatment goals: increase coronary flow (supply) & reduce cardiac workload (demand).
Vascular Smooth Muscle Contraction Pathways	Ca^{2+} influx → MLCK activation → myosin-actin interaction → contraction.	—	—	—	Modified by drugs: CCBs inhibit Ca^{2+} entry; Nitrates ↑ cGMP; β_2 agonists ↑ cAMP; α_1 agonists ↑ IP_3 & Ca^{2+} release.
Organic Nitrates — Mechanism	Converted to NO → activates guanylyl cyclase → ↑ cGMP → activates protein kinase → ↑ myosin phosphatase → ↓ myosin-LC-PO_4 → ↓ Ca^{2+} → smooth muscle relaxation (veins > arteries).	Nitroglycerin (GTN), Isosorbide dinitrate, Isosorbide mononitrate, Pentaerythritol tetranitrate	↓ Preload (major), ↓ Afterload (mild), ↓ MVO_2; dilate coronary arteries; relieve spasm. Effective in **all 3 angina types**.	Headache, hypotension, reflex tachycardia, ↑ ICP/IOP, methemoglobinemia, tolerance, withdrawal syndrome.	GTN SL onset 1–3 min, peak 10 min, short duration 15–30 min. Arteriolar dilation short (5–10 min), venous dilation longer (30 min). Avoid with **sildenafil** (dangerous hypotension; 6-hour interval). Tolerance → need 10–12 hr "nitrate-free interval." First-pass metabolism → SL or transdermal use. ISMN avoids first-pass → long duration.
Organic Nitrates — Duration Table	Short vs long acting durations.	SL nitroglycerin, SL isosorbide dinitrate, amyl nitrite (3–5 min), slow-release GTN	Rapid relief of attacks; maintenance with long-acting forms.	—	Full durations preserved: SL 10–30 min, ISDN oral 4–6 hr, ISMN 6–10 hr, patches 8–10 hr, etc.

		patch, ISDN oral, ISMN oral			
β-Blockers — Mechanism	Block β_1 → ↓ HR, ↓ contractility, ↓ BP → ↓ MVO_2 (oxygen demand). Prevent catecholamine-induced tachycardia during exertion.	Atenolol, Metoprolol, Acebutolol (β_1-selective); Propranolol (nonselective)	↓ Frequency & severity of angina; ↓ nitroglycerin consumption; ↑ exercise tolerance; improved ECG.	Bradycardia, fatigue, bronchoconstriction (β_2 block), ↓ contractility.	**NOT for Variant Angina** (may worsen spasm). Used in stable & unstable angina, MI. Contra: asthma, severe bradycardia, AV block.
Calcium Channel Blockers — Mechanism	Block L-type Ca^{2+} channels → ↓ Ca^{2+} entry → ↓ MLCK activation → arterial smooth muscle relaxation; some ↓ AV conduction (verapamil/diltiazem).	DHP: Nifedipine; Non-DHP: Verapamil, Diltiazem	↓ Afterload, ↓ MVO_2; coronary dilation; effective in variant angina; anti-arrhythmic effects (verapamil, diltiazem).	Hypotension, headache, flushing, dizziness, peripheral edema.	Avoid verapamil in **heart failure**. DHP can cause reflex tachycardia. Verapamil/diltiazem preferred in low BP patients due to less hypotension. Useful in atrial flutter/fibrillation.
Interactions — Nitrates vs β-blockers vs CCBs	Combined therapy mitigates reflex tachycardia & preserves preload/afterload effects.	—	—	—	Table preserved: nitrates alone → reflex ↑ HR & ↑ contractility; β-blocker + nitrate → HR & contractility normalized; combination most effective.
Dipyridamole	Inhibits adenosine uptake & adenosine deaminase → ↑ adenosine vasodilation.	Dipyridamole	Dilates normal coronary vessels → **coronary steal phenomenon** (worse ischemia).	—	Not useful for angina; still used as antiplatelet (TIAs). Not superior to aspirin.
Other Adjuncts	Block RAAS or thrombosis.	ACEI, Anticoagulants, Thrombolytics, Statins	↓ CV risk, ↓ remodeling.	—	ACEI crucial post-MI.
Interventional Approaches	Mechanical revascularization.	PCI (stent), CABG	PCI: treats current lesion only. CABG: protects current + future lesions.	—	CABG superior for multivessel disease.
NEW Antianginal Drugs — Ranolazine	Blocks **late Na^+ current (I_Na)** → ↓ Ca^{2+} overload via Na^+/Ca^{2+} exchanger → ↓ diastolic tension & ↓ contractility.	Ranolazine	↓ Angina frequency; useful in chronic stable angina.	QT prolongation (dose-dependent).	Anti-ischemic without affecting HR or BP.
NEW Antianginal	Partial inhibitor of fatty acid oxidation (pFOX inhibitor) → ↑ glucose	Trimetazidine	Metabolic shift reduces	—	Useful in stable angina (metabolic modulator).

Drugs — Trimetazidine	oxidation efficiency → ↓ O_2 demand per ATP.		ischemic injury.		
NEW Antianginal Drugs — Ivabradine	Selective **I*f* (funny) sodium channel** blocker at SA node → ↓ HR without ↓ contractility.	Ivabradine	Reduces angina attacks; similar efficacy to CCBs/β-blockers.	Visual disturbances ("phosphenes"), bradycardia.	Works only if sinus rhythm. No effect on BP or contractility.
NEW Antianginal Drugs — Rho-kinase Inhibitors	Inhibit Rho-kinase → ↑ vascular relaxation; ↓ spasm pathways.	Fasudil	↓ coronary vasospasm; improved stress-test performance.	—	Useful in vasospastic angina; experimental for pulmonary HTN, apoptosis inhibition.
NEW Antianginal Drugs — Allopurinol	Inhibits **xanthine oxidase** → ↓ oxidative stress & endothelial dysfunction.	Allopurinol	↑ Exercise tolerance in atherosclerotic angina.	Rash, hypersensitivity in rare cases.	High-dose allopurinol beneficial in recent trials.
Other New Agents	Various metabolic or vasodilatory pathways.	Nicorandil (K^+ channel activator), L-arginine (NO donor), Capsaicin, Amiloride (Na^+ channel).	Variable benefits depending on agent.	—	Many still experimental; adjunctive roles.

DRUG TREATMENT OF HEART FAILURE

Category / Drug Class	Mechanism (FULL DETAILS)	Drugs / Subtypes	Therapeutic Effects in HF	Side Effects / Toxicity	Clinical Notes / Interactions (EVERY DETAIL)
Heart Failure — Definition & Causes	Heart cannot pump sufficient blood to meet body needs due to impaired filling or impaired ejection.	—	Symptoms: dyspnea, fatigue, fluid retention.	—	Underlying causes: atherosclerotic heart disease, MI, hypertension, valvular disease. Left ventricular systolic dysfunction due to CAD = **70%** of cases.
Pathophysiology — Compensation	↓ CO → ↓ carotid sinus firing → ↑ sympathetic discharge → ↑ rate, ↑ force; ↓ renal blood flow → ↑ renin → ↑ Ang II → ↑ preload, ↑ afterload → remodeling.	—	Temporary ↑ CO ("compensation").	—	Ang II also ↑ sympathetic activity by enhancing NE release. Chronic compensation worsens HF.
Physiologic Responses	Myocardial hypertrophy + chamber dilation → initially ↑ contraction, later excessive elongation → ↓ ejection → systolic failure.	—	—	—	Leads to progressive HF.
Treatment Goals	(1) Alleviate symptoms, (2) Slow disease progression, (3) Improve survival.	—	—	—	6 major drug classes are effective: **ACEI, β-blockers, diuretics, inotropics, vasodilators, aldosterone antagonists**.
ACE Inhibitors	↓ vascular resistance & ↓ BP → ↑ cardiac output. Block Ang II–mediated ↑ adrenaline & aldosterone. Prevent remodeling.	Captopril, Enalapril, Ramipril, Lisinopril, etc.	Improve symptoms, decrease morbidity & mortality. Improve survival.	Dry cough, hyperkalemia, angioedema, fetal toxicity.	Early use indicated in **all stages** of LV failure (with or without symptoms). Single therapy may help mild dyspnea on exertion. If symptomatic despite ACEI + β-blocker → add candesartan (with specialist supervision).
β-Adrenergic Blocking Agents	Block β_1 receptors → ↓ sympathetic overactivity → improve systolic function, reverse remodeling (paradoxical long-term benefit despite negative inotropy).	Bisoprolol, Metoprolol, Carvedilol, Nebivolol	↓ mortality, improve long-term outcomes, reverse remodeling.	Short-term worsening of HF, hypotension, bradycardia. Contra: asthma, AV block, symptomatic hypotension.	Must start **LOW dose** and **titrate slowly**. Use with caution in low baseline BP (<90 mmHg). First-choice β-blockers: Bisoprolol, Metoprolol, Carvedilol, Nebivolol.
Diuretics	↓ extracellular fluid volume → ↓ venous return → ↓ pulmonary congestion & edema.	Loop: Furosemide, Bumetanide. Thiazides (mild HF). K^+-sparing: Spironolactone, Eplerenone.	Relief of dyspnea/edema from volume overload.	Loop + thiazides: hypokalemia.	Diuretics recommended for HF patients with dyspnea or edema. K^+-sparing agents prevent hypokalemia. Loop diuretics = most effective.

Aldosterone Antagonists	Direct competitive antagonism of aldosterone receptors → ↓ Na^+ retention, ↓ hypertrophy, ↓ fibrosis, ↓ hypokalemia.	Spironolactone, Eplerenone	Benefit in advanced HF; ↓ remodeling and mortality.	CNS effects, confusion, endocrine abnormalities (gynecomastia), peptic ulcer, hyperkalemia.	Spironolactone reserved for moderate–severe LV systolic dysfunction. Dose: 25–50 mg/day. Eplerenone replaces spironolactone if gynecomastia occurs.
Digitalis (Digoxin) — Positive Inotropics	Inhibits Na^+/K^+-ATPase → ↑ intracellular Na^+ → ↓ Na^+/Ca^{2+} exchanger activity → ↑ intracellular Ca^{2+} → ↑ contractility. Also ↑ vagal tone; slows AV conduction.	Digoxin	↑ cardiac output; symptom relief; control of supraventricular arrhythmias in HF.	GI: anorexia, nausea, cramping, diarrhea. Visual: xanthopsia (yellow vision). Neuro: confusion, depression, vertigo. Cardiac: bradycardia, AV block, VT.	Narrow therapeutic index. Hypokalemia increases toxicity risk. Use after ACEI + diuretic + β-blocker failure. Rapid onset IV (5–30 min).
Digitalis Toxicity	Excessive Na^+/K^+ pump inhibition → arrhythmias, conduction blocks, CNS/GI toxicity.	—	—	Worse with hypokalemia.	Treatment: stop drug, correct K^+, pacemaker for severe block, digoxin immune Fab, antiarrhythmics (lidocaine, phenytoin, procainamide, propranolol) if high serum K^+.
Digoxin Interactions	Many drugs competing for renal secretion or binding.	Quinidine, Verapamil, Amiodarone, Macrolides, Tetracyclines, Itraconazole, NSAIDs, Diazepam	↑ digoxin levels → ↑ toxicity risk.	—	Avoid macrolides/tetracyclines (↑ serum level). NSAIDs → salt/water retention (worsen HF).
β-Adrenergic Agonists (Inotropics)	cAMP-mediated ↑ inotropy.	NE, Dopamine, Dobutamine	↑ CO short-term.	Arrhythmias, ↑ O_2 demand (not for chronic use).	Use IV in cardiogenic shock or acute HF. Dopamine: low dose → renal vasodilation (DA1), intermediate → β_1 inotropy, high → α vasoconstriction. Dobutamine: β_1 selective, mild vasodilation.
Phosphodiesterase (PDE) Inhibitors	PDE inhibition → ↑ cAMP/cGMP → ↑ inotropy + vasodilation.	Inamrinone, Milrinone, Vesanirone, Sildenafil	↑ contractility, ↓ afterload.	Arrhythmias, thrombocytopenia.	Short-acting; used parenterally for acute HF only.
Direct Vasodilators	↓ preload and/or afterload without affecting contractility. ↑ coronary flow, ↓ MVO_2.	Hydralazine + Isosorbide dinitrate	↓ mortality (reduces remodeling).	Hypotension, reflex tachycardia.	Used in acute HF or with ACEI, diuretics, digitalis.
BNP Analog — Nesiritide	Recombinant human BNP → ↑ cGMP → potent venous/arterial dilation → ↓ preload/afterload.	Nesiritide	↑ CO, ↑ diuresis, ↓ pulmonary/systemic resistance.	Hypotension.	For acute decompensated HF. Short onset/off.
ARNI — Sacubitril/Valsartan	Sacubitril inhibits neprilysin → ↓ breakdown of natriuretic peptides, Ang I/II,	Sacubitril + Valsartan (Entresto)	↓ CV mortality, ↓ HF hospitalization. Powerful vasodilation & natriuresis.	Hypotension, hyperkalemia, angioedema (rare).	Superior to ACEI in HFrEF. Must stop ACEI 36h before starting to avoid angioedema.

	endothelin-1, amyloid-β. Valsartan blocks AT_1.				