Newer Drug Therapies for Hypertension

Recent advancements in hypertension treatment have led to the development of novel drug classes and combination therapies to improve blood pressure control and reduce cardiovascular risks.

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1. Angiotensin Receptor–Neprilysin Inhibitors (ARNIs)
Example: Sacubitril/Valsartan (Entresto)

- **Mechanism:**
  - Combines **Valsartan (ARB)** with **Sacubitril**, which inhibits neprilysin (an enzyme that breaks down vasodilators).
  - Increases levels of **natriuretic peptides**, promoting vasodilation and sodium excretion.
- **Use:**
  - Approved for **heart failure**, but shows promise in hypertension, especially in high-risk patients.
- **Advantages:**
  - More effective in reducing BP than ARBs alone.
  - Beneficial for heart and kidney protection.

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2. Dual Endothelin Receptor Antagonists
Example: Aprocitentan

- **Mechanism:**
  - Blocks **endothelin receptors (ET-A & ET-B)**, preventing blood vessel constriction.
- **Use:**
  - **Resistant hypertension** (when BP remains high despite using 3+ drugs).
- **Advantages:**
  - Effective for patients who do not respond to conventional therapies.

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3. Aldosterone Synthase Inhibitors
Example: Baxdrostat (Investigational)

- **Mechanism:**

- Inhibits **aldosterone synthesis**, reducing sodium retention and blood pressure.

- **Use:**
  - **Resistant hypertension** and patients with **primary aldosteronism**.
- **Advantages:**
  - Selective action, reducing side effects seen with older aldosterone blockers (e.g., Spironolactone).

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4. Nonsteroidal Mineralocorticoid Receptor Antagonists (MRAs)
Example: Finerenone

- **Mechanism:**
  - Blocks **mineralocorticoid receptors**, reducing salt and water retention while preventing fibrosis.
- **Use:**
  - Approved for **chronic kidney disease (CKD) with hypertension and diabetes**.
- **Advantages:**
  - Less risk of **high potassium** compared to older MRAs like Spironolactone.

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5. Centrally Acting Amino Acid–Based Drugs
Example: Moxonidine

- **Mechanism:**
  - Stimulates **imidazoline receptors in the brain**, reducing sympathetic nervous activity and lowering BP.
- **Use:**
  - **Hypertension with metabolic syndrome** (helps improve insulin sensitivity).
- **Advantages:**
  - Fewer side effects than older central-acting drugs like Clonidine.

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6. Novel Vasodilators (Soluble Guanylate Cyclase Stimulators)
Example: Vericiguat

- **Mechanism:**

- Stimulates **soluble guanylate cyclase (sGC)**, enhancing nitric oxide effects and dilating blood vessels.

- **Use:**
  - Approved for **heart failure**, but under study for hypertension.
- **Advantages:**
  - Works differently from traditional vasodilators, offering a new treatment option for resistant cases.

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7. New Drug Combinations for Better Control

- **Quadpill (Low-Dose Four-Drug Combination)**
  - Contains **low doses of four antihypertensive drugs** (ACE inhibitor, ARB, diuretic, CCB).
  - **Advantages:** Better BP control with fewer side effects than high-dose single drugs.

Future Directions in Hypertension Therapy

- **Gene Therapy:** Research into targeting genes involved in BP regulation.
- **RNA-based Drugs:** Potential to block hypertension-related proteins.
- **Personalized Medicine:** AI-driven BP monitoring to tailor treatment.