Comparison of Atypical Antipsychotics (United States)

modified April 2025

The chart below compares atypicals in regard to **adult** indications and dosing, metabolic side effects, sedation, CYP metabolism, and cost. Prescribers can bill for IM antipsychotic injections under their supervision using CPT code 96372 and add the medication code.

NOTE: *Usual or target daily ADULT dosage range may not include initial and maximum doses. Use lowest effective dose. Dosing in special populations (e.g., renal impairment, geriatrics) is not included. Maximum doses of oral aripiprazole, brexpiprazole, cariprazine, lurasidone, olanzapine, olanzapine/samidorphan, paliperidone, quetiapine *XR*, and risperidone are approved for once-daily administration. Total daily doses of asenapine, iloperidone, quetiapine IR (except for bipolar depression), and ziprasidone are divided twice daily. Clozapine doses above 12.5 mg should be divided.

Generic (Brand)/ Cost[b]	FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*,[a]	Notable Adverse Effects[4,a,c]				CYP450 Metabolism[a]
		Weight Gain	Diabetes Risk	Dys-lipidemia	Sedation	
Aripiprazole (Abilify, generics; Opipza oral film) 10 mg tablet ~$10 Opipza 10 mg oral film ~$2,300 Oral solution and orally disintegrating tablet also available.	Schizophrenia: 10-15 mg Bipolar I disorder* (manic or mixed episodes): 15 mg (monotherapy or with lithium or valproate) *note: Opipza is not approved for bipolar disorder Major depression (adjunct to antidepressants): 5-10 mg	Low	Low	Low	Low (may cause insomnia[2])	**CYP3A4, CYP2D6** (dosage adjustments do not apply to major depression) Reduce dose by 50% with strong CYP3A4 or strong CYP2D6 inhibitors, and in known CYP2D6 poor metabolizers. Reduce dose by 75% with strong CYP2D6 plus strong CYP3A4 inhibitors, or in CYP2D6 poor metabolizers taking a strong CYP3A4 inhibitor. Use twice the usual dose (increase over one to two weeks) with strong CYP3A4 inducers.

Generic (Brand)/ Cost[b]	**FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*[,a]**	**Notable Adverse Effects[4,a,c]**				**CYP450 Metabolism[a]**
		Weight Gain	**Diabetes Risk**	**Dys-lipidemia**	**Sedation**	
Aripiprazole (Abilify Asimtufii) 960 mg/ two months ~$5,800	Schizophrenia or Bipolar I maintenance: 960 mg every two months IM (gluteal). Establish tolerability with oral aripiprazole before use. Continue oral antipsychotic for 14 days after first dose, then stop. Missed dose: if >14 weeks have elapsed since the last injection, restart oral aripiprazole for 14 days with the injection.	Low	Low	Low	Low	**CYP3A4, CYP2D6** CYP450 modulators added for >14 days may require dosage changes. Dose is 720 mg every two months with strong CYP3A4 or strong CYP2D6 inhibitors, and in CYP2D6 poor metabolizers. Avoid with CYP3A4 inducers, concomitant use of a strong CYP2D6 inhibitor plus a strong CYP3A4 inhibitor, and in CYP2D6 poor metabolizers taking a CYP3A4 inhibitor.
Aripiprazole (Abilify Maintena long-acting injection) 400 mg ~$2,900	Schizophrenia: 400 mg IM (gluteal or deltoid) once monthly. Continue oral agent for 14 days after first dose, then stop. **Missed dose**: If >6 weeks elapse since last dose (>5 weeks if 2nd or 3rd dose is missed), restart oral aripiprazole x 14 days with the next dose.	Low	Low	Low	Low	**CYP3A4, CYP2D6** CYP450 modulators added for >14 days may require dosage changes. Reduce dose with strong CYP2D6 and/or CYP3A4 inhibitors. Reduce dose in CYP2D6 poor metabolizers taking a CYP3A4 inhibitor. Avoid with CYP3A4 inducers.

Generic (Brand)/ Cost[b]	**FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*[,a]**	**Notable Adverse Effects[4,a,c]**				**CYP450 Metabolism[a]**
		Weight Gain	**Diabetes Risk**	**Dys-lipidemia**	**Sedation**	
Aripiprazole lauroxil Aristada long-acting injection 662 mg ~$2,400 Aristada Initio (for loading) 675 mg x 1 ~$2,400	Schizophrenia: 441 mg IM (gluteal or deltoid), 662 mg (gluteal), or 882 mg (gluteal) once monthly; 882 mg (gluteal) once every 6 weeks; or 1,064 mg every 2 months (gluteal). Continue corresponding oral aripiprazole dose for 21 days after first dose, then stop. Alternatively, load with Aristada Initio 675 mg IM plus oral aripiprazole 30 mg x 1. Can start Aristada on same day or up to 10 days later. **Missed dose**: If >6 to ≤7 weeks (441 mg), >8 to ≤12 weeks (662 mg and 882 mg), or >10 to ≤12 weeks (1,064 mg) since last dose, restart oral aripiprazole x 7 days with next dose, or give with Aristada Initio x 1. If >7 weeks (441 mg) or >12 weeks (662 mg, 882 mg, and 1,064 mg) since last dose, restart oral aripiprazole x 21 days with next dose, or give with Aristada Initio 675 mg x 1 plus oral aripiprazole 30 mg x 1.	Low	Low	Low	Low	**CYP3A4, CYP2D6** Aristada: CYP450 modulators added for >14 days may require dosage changes. Reduce dose with strong CYP3A4 or CYP2D6 inhibitors. Avoid doses >441 mg with concomitant use of a strong CYP2D6 inhibitor AND a strong CYP3A4 inhibitor. Dosage increase may be needed with strong CYP3A4 inducers. Dose reduction may be needed in CYP2D6 poor metabolizers. Aristada Initio: Avoid with strong CYP2D6 inhibitors; with strong CYP3A4 inhibitors; with strong CYP3A4 inducers; and in CYP2D6 poor metabolizers.
Asenapine (Saphris, generics) 10 mg twice daily ~$210	Schizophrenia: 10 mg (acute), 10-20 mg (after one week) Bipolar I disorder (manic or mixed episodes and maintenance): 10-20 mg (monotherapy, or with lithium or valproate [acute treatment]) • For sublingual use. Avoid food/drink for 10 min afterward.	Moderate	Moderate	Moderate	Moderate	**CYP1A2, CYP3A4 (minor), CYP2D6 (minor)** Weak CYP2D6 inhibitor. Consider dose reduction with strong CYP1A2 inhibitors.

Generic (Brand)/ Cost[b]	**FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*[,a]**	**Notable Adverse Effects[4,a,c]**				**CYP450 Metabolism[a]**
		Weight Gain	**Diabetes Risk**	**Dys-lipidemia**	**Sedation**	
Asenapine (Secuado) All patch strengths ~$1,500	Schizophrenia: 3.8 to 5.7 mg (Doses of 7.6 mg can be used, but are unlikely to provide additional benefit, and may increase adverse effects.) • Patch applied once daily.	Moderate	Moderate	Moderate	Moderate	**CYP1A2, CYP3A4 (minor), CYP2D6 (minor)** Weak CYP2D6 inhibitor. Consider dose reduction with strong CYP1A2 inhibitors.
Brexpiprazole (Rexulti) All tablet strengths ~$1,500	Schizophrenia: 2-4 mg Major depressive disorder (adjunct to antidepressants): 2 mg Agitation associated with Alzheimer's dementia: 2 mg	Low	Low	Moderate	Moderate	**CYP3A4, CYP2D6** Reduce dose by 50% with strong CYP2D6 inhibitors (not depression indication) or strong CYP3A4 inhibitors, and in CYP2D6 poor metabolizers. Reduce dose by 75% for patients taking a strong or moderate CYP2D6 inhibitor plus a strong or moderate CYP3A4 inhibitor. Reduce dose by 75% for CYP2D6 poor metabolizers taking a strong or moderate CYP3A4 inhibitor. Double the dose over one to two weeks with strong CYP3A4 inducers.

Generic (Brand)/ Cost[b]	**FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*[,a]**	**Notable Adverse Effects[4,a,c]**				**CYP450 Metabolism[a]**
		Weight Gain	**Diabetes Risk**	**Dys-lipidemia**	**Sedation**	
Cariprazine (Vraylar*)* All capsule strengths ~$1,500	Schizophrenia: 1.5-6 mg Bipolar I disorder (manic or mixed episodes): 3-6 mg Bipolar I disorder (depression): 1.5 to 3 mg Major depressive disorder (adjunct to antidepressants): 1.5 to 3 mg	Moderate	Low	Low	Moderate	**CYP3A4, CYP2D6 (minor)** Reduce dose by 50% with strong CYP3A4 inhibitors. Avoid with CYP3A4 inducers.
Clozapine[d] (Clozaril, etc, generics) 100 mg tablet three times daily ~$110 Oral suspension (Versacloz) and generic orally disintegrating tablet also available.	Schizophrenia (treatment-resistant): 300-450 mg Reducing suicidal behavior in schizophrenia & schizoaffective disorder: 300-450 mg **NOTE: initial dose is 12.5 mg once or twice daily (for both indications).**	High	High	High	High	**CYP1A2, CYP3A4, CYP2D6** Reduce dose by one-third with strong CYP1A2 inhibitors. Not recommended with strong CYP3A4 inducers. Consider dose reduction with weak or moderate CYP1A2 inhibitors, CYP2D6 or CYP3A4 inhibitors, and in CYP2D6 poor metabolizers.
Iloperidone (Fanapt) 6 mg tablet twice daily ~$2,300	Schizophrenia: 12-24 mg	Moderate	Moderate	Low	Moderate	**CYP3A4, CYP2D6** Reduce dose with strong CYP2D6 or strong CYP3A4 inhibitors.

Generic (Brand)/ Cost[b]	**FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*[,a]**	**Notable Adverse Effects[4,a,c]**				**CYP450 Metabolism[a]**
		Weight Gain	**Diabetes Risk**	**Dys-lipidemia**	**Sedation**	
Lumateperone (Caplyta) All capsule strengths ~$1,700	Schizophrenia: 42 mg Bipolar I or II depression: 42 mg	Low	Low to moderate	Low	Moderate	**CYP1A2, CYP2C8, CYP3A4** Avoid with CYP3A4 inducers. Reduce dose with strong or moderate CYP3A4 inhibitors.
Lurasidone (Latuda, generics) 40 mg tablet ~$20	Schizophrenia: 40-160 mg Bipolar I depres3sion (monotherapy or with lithium or valproate): 20-120 mg • Take with food (at least 350 kcal).	Low	Low[6]	Low[6]	Moderate	**CYP3A4** Contraindicated with strong CYP3A4 inhibitors or inducers. Reduce dose by 50% with moderate CYP3A4 inhibitors. Increase dose with moderate CYP3A4 inducers.
Olanzapine (Zyprexa, generics) 10 mg tablet ~$10 Injection: ~$30/10 mg Generic orally disintegrating tablet available.	Schizophrenia: 10 mg Bipolar I disorder (manic or mixed episodes and maintenance): 5-20 mg (monotherapy, or with lithium or valproate [acute treatment]) Bipolar I depression, with fluoxetine: 5-12.5 mg Depression (treatment-resistant), with fluoxetine: 5-20 mg Zyprexa IntraMuscular, agitation associated with psychosis or bipolar I mania: 10 mg (lower dose [5 mg, 7.5 mg] may be given). May repeat dose in 2 hours. A third dose may be given no sooner than 4 hours after the second dose.	High	High	High	High	**CYP1A2, CYP2D6**

Generic (Brand)/ Cost[b]	**FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*[,a]**	**Notable Adverse Effects[4,a,c]**				**CYP450 Metabolism[a]**
		Weight Gain	**Diabetes Risk**	**Dys-lipidemia**	**Sedation**	
Olanzapine pamoate (Zyprexa Relprevv long-acting injection) 300 mg ~$840	Schizophrenia: Establish tolerability and target dose with oral olanzapine first. Patients can switch to Zyprexa Relprevv with or without tapering.[1] Zyprexa Relprevv is initiated with an 8-week loading regimen and is dosed every 2 or 4 weeks IM (gluteal). Available only through a **restricted distribution program** requiring prescriber, facility, patient, and pharmacy enrollment. **Missed dose**: see footnote e.	High	High	High	High Rare risk of post-injection sedation (including coma) and/or delirium. Monitor for at least 3 hours post-dose.	**CYP1A2, CYP2D6**
Olanzapine/ samidorphan (Lybalvi) 15 mg/10 mg tablet ~$1,600	Schizophrenia: 10 mg/10 mg to 20 mg/10 mg Bipolar I (manic or mixed episodes [acute treatment or maintenance]): 5 mg/10 mg to 20 mg/10 mg Bipolar I (adjunct to lithium or valproate for manic or mixed episodes [acute treatment]): 10 mg/10 mg to 20 mg/10 mg	High	High	High	High	**CYP1A2, CYP2D6, CYP3A4** Avoid strong CYP3A4 inducers. It may be necessary to: • reduce the dose of the olanzapine component with strong CYP1A2 inhibitors. • increase the dose of the olanzapine component with CYP1A2 inducers.
Paliperidone (Invega, generics) 6 mg extended-release tablet ~$70	Schizophrenia: 3-12 mg Schizoaffective disorder: 3-12 mg (monotherapy or adjunct to mood stabilizers or antidepressants)	Moderate	Low	Moderate	Low	**CYP2D6 (minor), CYP3A4 (minor)** It may be necessary to increase the dose if used with a strong inducer of both CYP3A4 and P-glycoprotein.

Generic (Brand)/ Cost[b]	**FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*[,a]**	**Notable Adverse Effects[4,a,c]**				**CYP450 Metabolism[a]**
		Weight Gain	**Diabetes Risk**	**Dys-lipidemia**	**Sedation**	
Paliperidone palmitate (Invega Sustenna long-acting injection) 117 mg ~$1,800	Schizophrenia or schizoaffective disorder: IM monthly after 2 doses one week apart. Establish tolerability with oral paliperidone or risperidone before use. Taper oral agent with first dose. When switching from a long-acting injectable, start in place of the next scheduled dose. **Missed maintenance dose**: resume regular monthly dosing if up to 2 weeks late. Details on handling other missed dosing scenarios are provided in the product labeling.	Moderate	Low	Moderate	Low	**CYP2D6 (minor), CYP3A4 (minor)** Avoid CYP3A4 and/or P-glycoprotein inducers, if possible.
Paliperidone palmitate (Invega Trinza long-acting injection) 410 mg ~$1,800	Schizophrenia, after adequate treatment with Invega Sustenna for at least 4 months: IM every 3 months. Dose depends on previous Invega Sustenna dose. **Missed maintenance dose**: can give up to two weeks early or up to 1 month late. Details on handling missed doses are provided in the product labeling.	Moderate	Low	Moderate	Low	**CYP2D6 (minor), CYP3A4 (minor)** Avoid CYP3A4 and/or P-glycoprotein inducers, if possible.
Paliperidone palmitate (Invega Hafyera long-acting injection 1,092 mg ~$2,400	Schizophrenia, after adequate treatment with Invega Sustenna for at least 4 months or Invega Trinza for at least one 3-month cycle: IM every 6 months. Dose depends on previous Invega Sustenna or Invega Trinza dose. **Missed maintenance dose**: Can give up to two weeks early or 3 weeks late. Details on handling missed doses are provided in the product labeling.	Moderate	Low	Moderate	Low	**CYP2D6 (minor), CYP3A4 (minor)** Avoid CYP3A4 and/or P-glycoprotein inducers, if possible.

Generic (Brand)/ Cost[b]	**FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*[,a]**	**Notable Adverse Effects[4,a,c]**				**CYP450 Metabolism[a]**
		Weight Gain	**Diabetes Risk**	**Dys-lipidemia**	**Sedation**	
Quetiapine (Seroquel, generics) 200 mg tablet twice daily ~$15	Schizophrenia: 150-750 mg Bipolar depression (bipolar I and II): 300 mg Bipolar mania or bipolar I maintenance (monotherapy [acute] or as an adjunct to lithium or valproate [acute, maintenance]): 400-800 mg	Moderate	Moderate	High	High	**CYP3A4** Reduce dose to one-sixth with strong CYP3A4 inhibitors. Increase dose up to five-fold with a strong CYP3A4 inducer taken for >7 to 14 days.
Quetiapine (Seroquel XR, generics) 400 mg extended-release tablet ~$15	Schizophrenia: 400-800 mg Bipolar depression (acute): 300 mg Bipolar I manic or mixed episode (monotherapy [acute] or as an adjunct to lithium or valproate [acute, maintenance]): 400-800 mg Major depressive disorder (adjunct to antidepressants): 150-300 mg • Take without food or with a light meal (about 300 kcal).	Moderate	Moderate	High	High	**CYP3A4** Reduce dose to one-sixth with strong CYP3A4 inhibitors. Increase dose up to five-fold with a strong CYP3A4 inducer taken for >7 to 14 days.
Risperidone (Risperdal, generics) 4 mg tablet ~$90 Generic oral solution and orally disintegrating tablet available.	Schizophrenia: 4-8 mg Bipolar I disorder (acute manic or mixed episodes; monotherapy or as an adjunct to lithium or valproate): 1-6 mg	Moderate	Moderate	Low	Moderate	**CYP2D6, CYP3A4 (minor)**[2] Reduce initial dose and do not exceed 8 mg max with strong CYP2D6 inhibitors. Dose can be doubled for use with CYP3A4 or P-glycoprotein inducers.

Generic (Brand)/ Cost[b]	**FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*[,a]**	**Notable Adverse Effects[4,a,c]**				**CYP450 Metabolism[a]**
		Weight Gain	**Diabetes Risk**	**Dys-lipidemia**	**Sedation**	
Risperidone (Perseris long-acting injection) 90 mg ~$2,200	Schizophrenia: 90-120 mg once monthly (subcutaneous in the abdomen or upper arm). Establish tolerability with oral risperidone before starting. Perseris 90 mg monthly equals ~3 mg oral risperidone once daily; Perseris 120 mg equals ~4 mg oral risperidone once daily. **Missed dose**: restart as soon as possible.	Moderate	Moderate	Low	Moderate	**CYP2D6, CYP3A4 (minor)**[2] Consider dose reduction to 90 mg beginning two to four weeks before starting a strong CYP2D6 inhibitor. Consider increasing the dose to 120 mg with CYP3A4 inducers. Additional oral risperidone may be needed.
Risperidone (Risperdal Consta long-acting injection) 25 mg ~$1,300	Schizophrenia: 25 mg IM every 2 weeks Bipolar I maintenance (monotherapy or as an adjunct to lithium or valproate): 25 mg IM every 2 weeks • Continue oral agent for 3 weeks after first dose, then discontinue. **Missed dose**, and <4 consecutive doses received: Give injection, plus oral agent for 3 weeks.[3] **Missed dose**, and 4 or more consecutive doses received: If only 3-6 weeks have passed since last injection, give injection alone. If >6 weeks have passed since last injection, give injection, plus oral agent for 3 weeks.[3]	Moderate	Moderate	Low	Moderate	**CYP2D6, CYP3A4 (minor)**[2] Consider dose reduction to 25 mg beginning two to four weeks before starting a strong CYP2D6 inhibitor. Consider initiating with 12.5 mg in patients already taking a strong CYP2D6 inhibitor. A dosage increase or additional oral risperidone may be needed with a strong CYP3A4 inducer.

Generic (Brand)/ Cost[b]	**FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*[,a]**	**Notable Adverse Effects[4,a,c]**				**CYP450 Metabolism[a]**
		Weight Gain	**Diabetes Risk**	**Dys-lipidemia**	**Sedation**	
Risperidone (Rykindo extended-release injectable suspension) 25 mg ~$1,200	Schizophrenia or Bipolar I maintenance (monotherapy or as an adjunct to lithium or valproate): 25 mg every 2 weeks IM (gluteal) Establish tolerability with oral risperidone before starting. Continue oral risperidone for 7 days after first dose, then stop.	Moderate	Moderate	Low	Moderate	**CYP2D6, CYP3A4 (minor)**[2] Consider dose reduction to 25 mg two to four weeks before starting a strong CYP2D6 inhibitor. A dosage increase or the addition of oral risperidone may be needed with a strong CYP3A4 inducer.
Risperidone (Uzedy) Extended-release injectable suspension 100 mg ~$2,600	Schizophrenia: 50 mg once monthly to 250 mg every two months. Dose is based on prior oral risperidone dose. 2 mg/day = 50 mg once monthly or 100 mg every 2 months.	Moderate	Moderate	Low	Moderate	**CYP2D6, CYP3A4 (minor)**[2] Consider dose reduction to 50 mg once monthly or 100 mg every 2 months before starting a strong CYP2D6 inhibitor. A dosage increase or the addition of oral risperidone may be needed with a strong CYP3A4 inducer.
Ziprasidone (Geodon, generics) 40 mg capsule twice daily ~$80 Injection ~$25/20 mg	Schizophrenia: 40-160 mg Bipolar I disorder (acute manic or mixed episodes, maintenance [adjunct to lithium or valproate]): 80-160 mg • Take with food. **Injection**: agitation associated with schizophrenia: 10 mg IM q 2 hrs or 20 mg q 4 hrs. Max 40 mg/day.	Low	Low	Low	Moderate	**CYP3A4, CYP1A2 (minor)**

a. **Per US product information**: Abilify (November 2022), Abilify Asimtufii (August 2023), Abilify Maintena (June 2020), Aristada (March 2021), Aristada Initio (March 2021), Opipza (August 2024), Saphris (October 2021), Secuado (November 2022), Rexulti (May 2023), Vraylar (December 2022), Clozaril (May 2023), Fanapt (February 2017), Caplyta (June 2023), Latuda (May 2022), Zyprexa and Zyprexa IntraMuscular (February 2021), Zyprexa Relprevv (November 2021), Lybalvi (May 2021), Invega (February 2021), Invega Sustenna (July 2022), Invega Trinza (August 2021), Invega Hafyera (August 2021), Seroquel (January 2022), Seroquel XR (January 2022), Risperdal (August 2022), Perseris (December 2022), Risperdal Consta (February 2021), Rykindo (May 2023), Uzedy (May 2023), Geodon (February 2022).
b. Wholesale acquisition cost (US) per month (unless otherwise specified), for generic if available, of dose specified. Medication pricing by Elsevier, accessed April 2025.
c. **Extrapyramidal side effects** are low with aripiprazole, brexpiprazole, cariprazine, iloperidone, quetiapine, ziprasidone, and high with lurasidone, paliperidone, and risperidone.[4] **Hyperprolactinemia** (associated with sexual dysfunction, gynecomastia, and irregular periods) seems most common with risperidone and paliperidone, and lowest with aripiprazole, brexpiprazole, cariprazine, clozapine, lurasidone, and quetiapine.[4] **QT prolongation** risk varies among agents. Aripiprazole and lurasidone may pose relatively lower risk vs other agents, while iloperidone and ziprasidone may pose the highest risk.[4] See our chart, *Drug-Induced QT Prolongation: A Stepwise Approach*, for more information. **Anticholinergic effects** (e.g., dry mouth, constipation, difficult urination) may be most problematic with clozapine, cariprazine, olanzapine, and quetiapine,[4] and least with brexpiprazole, asenapine, and lurasidone.[7]
d. Clozapine is associated with severe neutropenia, seizures, and myocarditis. Hematological monitoring (absolute neutrophil count [ANC]) is required.[5]
e. *Zyprexa Relprevv*, **missed dose**: no specific dosing guidance is available; use clinical judgment. In some studies, up to 16 days (for every-2-week dosing) or 35 days (for every-4-week dosing) were allowed between doses. In practice, some patients can go >60 days between doses. The effective half-life of *Zyprexa Relprevv* is about 30 days.[1]

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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Angiotensin Receptor Blockers and Angiotensin-Converting Enzyme Inhibitors

modified April 2025

This resource provides two charts, *Comparison of Angiotensin Receptor Blockers* and *Comparison of Angiotensin-Converting Enzyme Inhibitors*, plus an algorithm, *Monitoring ACEIs and ARBs*. See **footnote b** for dosing in **special populations**.

--Information in charts is based on product labeling unless otherwise denoted.--

Comparison of Angiotensin Receptor Blockers (ARBS)

Medication	Initial Dose for approved Indications in Adults (also see footnote b)	Usual or Target Maintenance Dose (Adults)	Clinical Benefit (Based on A-1 or B-1 evidence in adults)	How Supplied/Cost of 30-day supply (generic, if available)[a]
Azilsartan (*Edarbi*)	**HTN**: 80 mg once daily[b] (Canada: 40 mg once daily)	80 mg once daily	None	40, 80 mg US: ~$235 (80 mg once daily) Canada: ~$42 (80 mg once daily) **With chlorthalidone** (*Edarbyclor*; not for volume-depleted patients): 40/12.5, 40/25
Candesartan (*Atacand*, generics)	**HTN**: 16 mg once daily[b] **HF**: 4 mg to 8 mg once daily[8]	**HTN**: 8 to 32 mg daily in one or two divided doses **HF**: 32 mg once daily	**HF**: Reduces HF hospitalization in patients with NYHA II-IV HF and LVEF ≤40% intolerant to ACE inhibitors (NNT = 13 patients for 2.8 years).[17] Reduces mortality (NNT = 33 patients for 3.3 years) and HF hospitalizations (NNT = 18 patients for 3.3 years) in patients with NYHA II-IV HF and LVEF ≤40% on standard therapies.[18] **Diabetic retinopathy**: reduces incidence (type 1 DM) and improves mild to moderate retinopathy (type 2 DM)[1,2]	4, 8, 16, 32 mg US: ~$100 (32 mg once daily) Canada: <$10 (32 mg once daily) **With HCT** (*Atacand HCT* [US]; *Atacand Plus* [Canada] indicated for HTN only; not for initial therapy; not for volume-depleted patients; no information on use in patients with CrCl ≤30 mL/min [Canada: contraindicated]): 16/12.5, 32/12.5, 32/25 mg

Medication	Initial Dose for approved Indications in Adults (also see footnote b)	Usual or Target Maintenance Dose (Adults)	Clinical Benefit (Based on A-1 or B-1 evidence in adults)	How Supplied/Cost of 30-day supply (generic, if available)[a]
Irbesartan (*Avapro*, generics)	**HTN**: 150 mg once daily[b] **Nephropathy (HTN, type 2 DM, elevated serum creatinine, and proteinuria)**: 300 mg once daily (Canada: 150 mg once daily)[b]	**HTN**: 150 to 300 mg once daily **Nephropathy (type 2 DM)**: 300 mg once daily (Canada: 150 to 300 mg once daily)	**Nephropathy (type 2 DM)**: Reduce risk of progression to ESRD in patients with HTN (NNT = 27 patients for 2.5 years). Reduces risk of doubling of SCr (NNT = 15 patients for 2.5 years).[21]	75, 150, 300 mg US: ~$15 (300 mg once daily) Canada: ~$41 (300 mg once daily) **With HCT** (*Avalide*; indicated for HTN only; not for volume-depleted patients; not recommended if CrCl <30 mL/min): 150/12.5, 300/12.5
Losartan (*Cozaar*, generics; *Arbli* suspension)	**HTN with or without LVH**: 50 mg once daily[b] **Nephropathy (type 2 DM, elevated serum creatinine, and proteinuria) plus HTN**: 50 mg once daily[b] **HF (off-label)**: 25 to 50 mg once daily[8,b]	**HTN**: 50 to 100 mg once daily (divide BID for better control) **HTN/LVH**: 50-100 mg once daily **Nephropathy (type 2 DM):** 50-100 mg once daily **HF (off-label)**: 50 to 150 mg once daily[8]	**HTN with LVH**: Reduces incidence of stroke in patients with HTN and LVH (NNT = 50 patients for 4.8 years) compared to atenolol.[29] **Nephropathy (type 2 DM, elevated creatinine, and proteinuria)**: reduces risk of progression to ESRD (NNT = 17 patients for 3.4 years). Reduces risk of doubling of serum creatinine (NNT = 23 patients for 3.4 years).[19] **HF**: Reduces risk of CV death or HF hospitalization;[3] mortality similar to captopril[11]	25, 50, 100 mg; 10 mg/mL suspension (*Arbli*) US: <$10 (100 mg once daily) Canada: <$10 (100 mg once daily) **With HCT** (*Hyzaar*, *Hyzaar DS* [Canada]; indicated for HTN and HTN with LVH only; not recommended (US: as initial therapy) in liver impairment; not for volume-depleted patients (US); no information on use in patients with CrCl <30 mL/min [Canada: not recommended]): 50/12.5, 100/12.5, 100/25 mg

Medication	Initial Dose for approved Indications in Adults (also see footnote b)	Usual or Target Maintenance Dose (Adults)	Clinical Benefit (Based on A-1 or B-1 evidence in adults)	How Supplied/Cost of 30-day supply (generic, if available)[a]
Olmesartan (*Benicar* [US], *Olmetec* [Canada], generics)	**HTN**: 20 mg once daily[b]	**HTN**: 20 to 40 mg once daily[b]	None	5 (US), 20, 40 mg US: ~$12 (40 mg once daily) Canada: <$10 (40 mg once daily) **With HCT** (*Benicar HCT* [US], *Olmetec Plus* [Canada]; not for initial therapy; not for volume-depleted patients (US); no information on use in patients with CrCl ≤30 mL/min): 20/12.5, 40/12.5, 40/25 mg **With amlodipine** (*Azor*; not for initial therapy in liver impairment or age ≥75 years): 5/20, 10/20, 5/40, 10/40 mg **With HCT and amlodipine** (*Tribenzor*; not for initial therapy; avoid if CrCl ≤30 mL/min): 20/5/12.5, 40/5/12.5, 40/5/25, 40/10/12.5, 40/10/25 mg
Telmisartan (*Micardis*, generics)	Correct volume-depletion before starting. **HTN**: 40 mg once daily (Canada: 80 mg once daily)[b] **CV risk reduction (in patients unable to take ACE inhibitors)**: 80 mg once daily[b]	**HTN**: 40 to 80 mg once daily (Canada: 80 mg once daily) **CV risk reduction**: 80 mg once daily	**High CV risk**: reduces risk of CV events (MI, stroke, death) **Hemodialysis patients with HF**: added to ACEI, reduces all-cause and CV mortality, and heart failure hospitalization[5]	20, 40, 80 mg US: ~$20 (80 mg once daily) Canada: <$10 (80 mg once daily) **With HCT** (*Micardis HCT* [US], *Micardis Plus* [Canada]; indicated for HTN only; not for initial therapy; not for volume-depleted patients; not recommended if CrCl ≤30 mL/min): 40/12.5 (US), 80/12.5, 80/25 mg **With amlodipine** (*Twynsta*; not for initial therapy [US]: in patients ≥75 years of age or with liver impairment); not for volume-depleted patients): 40/5 mg, 40/10 mg, 80/5 mg, 80/10 mg

Medication	Initial Dose for approved Indications in Adults (also see footnote b)	Usual or Target Maintenance Dose (Adults)	Clinical Benefit (Based on A-1 or B-1 evidence in adults)	How Supplied/Cost of 30-day supply (generic, if available)[a]
Valsartan (*Diovan*, generics)	**HTN**: 80-160 mg once daily (Canada: 80 mg once daily) (non-volume-depleted patients) **HF (NYHA II to IV)**: 20 to 40 mg BID[8] (Canada: 40 mg BID[30]) **Post-MI with left ventricular dysfunction/failure**: 20 mg BID	**HTN**: 80 to 320 mg once daily **HF**: 160 mg BID **Post-MI**: 160 mg BID	**HTN with high CV risk**: reduces CV morbidity/mortality about as well as amlodipine[6] **HF**: reduces CHF hospitalization **Post-MI with left ventricular dysfunction/failure**: reduces CV mortality	40, 80, 160, 320 mg US: ~$25 (320 mg once daily) Canada: <$10 (320 mg once daily) **With HCT** (*Diovan HCT*; indicated for HTN only; not for initial therapy [Canada]; not for volume-depleted patients [US]: 80/12.5, 160/12.5, 160/25, 320/12.5, 320/25 mg **With amlodipine** (*Exforge* [US]; indicated for HTN only; not for volume-depleted patients; not for initial therapy in elderly or liver impairment): 5/160, 10/160, 5/320, 10/320 mg **With amlodipine and HCT** (*Exforge HCT* [US]; indicated for HTN only; not for initial therapy; not for volume-depleted patients): 5/160/12.5, 10/160/12.5, 5/160/25, 10/160/25, 10/320/25 mg

US product information used in preparation of this chart: *Edarbi* (April 2023), *Edarbyclor* (April 2023), *Atacand* (June 2020), *Atacand HCT* (May 2020), *Avapro* (September 2021), *Avalide* (July 2023), *Cozaar* (October 2021), Arbli (March 2025), *Hyzaar* (March 2023), *Benicar* (February 2022), *Benicar HCT* (February 2022), *Azor* (February 2022), *Tribenzor* (February 2022), *Micardis* (December 2022), *Micardis HCT* (December 2022), telmisartan/amlodipine (May 2019), *Diovan* (April 2021), *Diovan HCT* (August 2020), *Exforge* (April 2021), *Exforge HCT* (February 2021).
Canadian product monographs used in preparation of this chart: *Edarbi* (July 2021), *Edarbychlor* (July 2021), *Atacand* (February 2016), *Atacand Plus* (March 2023), *Avapro* (November 2022), *Avalide* (January 2023), *Cozaar* (July 2022), *Hyzaar* (November 2022), *Olmetec* (April 2021), *Olmetec* Plus (April 2021), *Micardis* (October 2022), *Micardis Plus* (October 2022), *Twynsta* (October 2022), *Diovan* (March 2023), *Diovan HCT* (February 2023).

a. US cost is wholesale average cost (WAC). Pricing by Elsevier, accessed October 2023.

b. Dosing of **ARBs** in **special populations.**

Azilsartan:

- **volume-depleted** patients: initial 40 mg once daily (US).

Candesartan:

- **volume-depleted** patients: consider a lower initial dose.
- **kidney impairment** (moderate to severe, or dialysis): consider 4 mg once daily initially for HTN (Canada).
- **liver impairment**: moderate liver impairment, 8 mg once daily initially for HTN (US); **severe liver impairment**, consider 4 mg once daily initially for HTN (Canada).

Irbesartan:

- **volume-depleted** patients: initial 75 mg once daily.
- **hemodialysis**: initial 75 mg once daily.

Losartan:

- **volume-depleted** patients: initial 25 mg once daily.
- **liver impairment** (mild to moderate): initial 25 mg once daily.

Olmesartan:

- **volume-depleted** patients: consider a lower initial starting dose.
- **kidney impairment** (mild to moderate): max dose 20 mg once daily (Canada). Not recommended in severe kidney impairment (Canada).
- **liver impairment** (moderate): a lower initial dose is recommended, and the max dose is 20 mg once daily (Canada).

Telmisartan:

- **liver impairment**: initial 40 mg once daily (Canada).

--Continue to the next section for the *Comparison of Angiotensin-Converting Enzyme Inhibitors* chart.—

Comparison of Angiotensin-Converting Emzyme Inhibitors (ACEIs)

Medication	Initial Dose for approved Indications in Adults (also see footnote b)	Usual or Target Maintenance Dose (Adults)	Clinical Benefit (Based on Level A evidence in adults)	How Supplied/Cost of 30-day supply (generic, if available)[a]
Benazepril (*Lotensin* [US], generics)	**HTN**: 10 mg once daily[b]	40 mg once daily (Canada: 20 mg once daily)(divide BID for better control) Limited experience with 80 mg/day[b] Canada: max dose 40 mg/day	**HTN with high CV risk**: benazepril/amlodipine reduces CV morbidity/mortality better than benazepril/HCT.[7]	5, 10, 20, 40 mg (US) US: <$12 (40 mg once daily) Canada: ~$42 (20 mg once daily) **With amlodipine** (*Lotrel* [US]; not for initial therapy; not for volume-depleted patients): 5/10, 5/20. 10/20. 10/40 mg **With HCT** (*Lotensin* HCT [US]; not for initial therapy; not for volume-depleted patients; no data in CrCl <30 mL/min.)**:** 10/12.5, 20/12.5, 20/25 mg
Captopril Take one hour before meals.	**HTN**: 25 mg BID to TID[b] **HF**: 6.25 mg TID[8] **Post-MI with LVEF ≤40%** (US): 6.25 mg x 1, then 12.5 mg TID **Nephropathy** (Type 1 DM, proteinuria, and retinopathy)(US): 25 mg TID[b]	**HTN**: 25 to 50 mg BID to TID (max 450 mg/day, divided) **HF**: 50 mg TID[8] **Post-MI**: 50 mg TID **Nephropathy**: 25 mg TID	**HF**: similar to losartan for improving survival and reducing risk of resuscitated arrest or sudden death.[11] **Post-MI**: improves survival and reduces CV morbidity/mortality in patients with LVD.[10] Reduces mortality (NNT = 63 for 4 weeks) and risk of HF (NNT = 59 for 4 weeks) after anterior wall infarct.[20] **Nephropathy**: reduces risk of doubling of SCr in type 1 DM patients with macroalbuminuria (NNT = 11 patients over 3 years)[9]	12.5, 25, 50, 100 mg US: ~$125 (50 mg TID) Canada: ~$55 (50 mg TID) **With HCT** (US): 25/15, 25/25, 50/15, 50/25 mg.

Medication	**Initial Dose for approved Indications in Adults (also see footnote b)**	**Usual or Target Maintenance Dose (Adults)**	**Clinical Benefit (Based on Level A evidence in adults)**	**How Supplied/Cost of 30-day supply (generic, if available)[a]**
Enalapril (*Vasotec*, generics)	**HTN**: 5 mg once daily[b] **HF**: 2.5 mg BID[8,b] (Canada: 1.25 to 2.5 mg BID[30]) **LVEF ≤35% (asymptomatic)**: 2.5 mg BID (Canada: 2.5 mg once daily)	**HTN**: 10 to 40 mg once daily (divide BID for better control) **HF**: 10 to 20 mg BID[8] (Canada: 10 mg BID, or 20 mg BID for NYHA IV[30]) **LVEF ≤35% (asymptomatic)**: 10 mg BID (Canada: 5 to 20 mg once daily or divided)	**HF**: reduces mortality and heart failure hospitalizations (NNT = 11 patients for 3.4 years) in patients with NYHA II and III HF.[14] Reduces mortality in patients with NYHA IV (NNT = 7 patients for 6 months).[16] **LVEF ≤35% (asymptomatic)**: Reduce development of overt HF (NNT = 11 patients for 3 years) and death from HF and HF hospitalization (NNT = 26 patients for 3 years).[15]	2.5 (US), 5, 10, 20 mg US: ~$37 (20 mg BID) Canada: ~$21 (20 mg BID) **With HCT** (*Vaseretic*; indicated for HTN only; not for initial therapy; not recommended if CrCl ≤30 mL/min): 10/25 mg
Fosinopril	**HTN**: 10 mg once daily **HF**: 5 to 10 mg once daily[8]	**HTN**: 20 to 40 mg once daily (divide BID for better control).[b] Some patients may benefit from 80 mg/day (US). **HF**: 40 mg once daily[8]	**HTN:** reduces major vascular events in patients with type 2 diabetes and hypertension (NNT = 15 patients for about 2.5 years) compared to amlodipine (secondary outcomes).[24] **HF:** reduces symptoms and HF hospitalization	10, 20, 40 mg (US) US: ~$11 (40 mg once daily) Canada: ~$17 (40 mg once daily) **With HCT** (US; indicated for HTN only; not for volume-depleted patients; not recommended if CrCl ≤30 mL/min): 10/12.5, 20/12.5 mg

Medication	Initial Dose for approved Indications in Adults (also see footnote b)	Usual or Target Maintenance Dose (Adults)	Clinical Benefit (Based on Level A evidence in adults)	How Supplied/Cost of 30-day supply (generic, if available)[a]
Lisinopril (*Zestril*, generics; *Qbrelis* oral solution)	**HTN**: 10 mg once daily[b] **HF**: 2.5 to 5 mg once daily[8,b] **Post-MI**: 5 mg within 24 hours of MI, then 5 mg after 24 hours, then 10 mg once daily[b]	**HTN:** 20 to 40 mg once daily. (Canada: 10 to 40 mg once daily)(80 mg has been used, but may not provide additional BP reduction).[b] **HF**: 20 to 40 mg once daily[8] (Canada: 20 to 35 mg once daily[30]) **Post-MI**: 10 mg once daily	**HTN:** reduces fatal/nonfatal MI in patients with hypertension plus one other CV risk factor as well as chlorthalidone or amlodipine.[13] **HF:** improves symptoms and NYHA classification **Post-MI**: reduce mortality post-MI in patients with DM (NNT = 27 patients for 6 weeks)[22]	2.5, 5, 10, 20, 30, 40 mg; 1 mg/mL oral solution (*Qbrelis*) US: <$10 (40 mg once daily) Canada: <$10 (20 mg once daily) **With HCT** (*Zestoretic*: indicated for HTN only; not recommended if CrCl ≤30 mL/min): 10/12.5. 20/12.5. 20/25 mg
Moexipril (US)	**HTN**: 7.5 mg once daily **CrCl ≤40 mL/min**: 3.75 mg once daily	**HTN**: 30 mg once daily (divide BID for better control) **CrCl ≤40 mL/min**: max daily dose 15 mg.	None	7.5, 15 mg US: ~$90 (30 mg once daily)
Perindopril (*Coversyl* [Canada], generics) Long duration of action.[30]	**HTN**: 4 mg once daily[b] **Stable CAD**: 4 mg once daily (>70 years of age: 2 mg once daily)[b] **HF (off-label)**: 2 mg once daily[8] (Canada: 2 to 4 mg once daily[30])	**HTN**: 4 to 8 mg once daily (divide BID for better control)(US: max 16 mg/day)[b] **Stable CAD**: 8 mg once daily[b] **HF (off-label)**: 8 to 16 mg once daily[8] (Canada: 4 to 8 mg once daily[30])	**Stable CAD**: reduces CV death, cardiac arrest, and **MI** in patients with stable CAD (NNT = 50 patients for 4.2 years)[23] **HF**: reduces symptoms and HF hospitalization[31]	2, 4, 8 mg US: ~$20 (8 mg once daily) Canada: <$10 (8 mg once daily) **With indapamide** (*Coversyl Plus*, *Coversyl Plus HD*, *Coversyl Plus LD* [Canada]: indicated for HTN only; not for initial therapy; contraindicated if eGFR <30 mL/min/1.73 m^2; *Coversyl Plus HD* is contraindicated if eGFR <60 mL/min/1.73 m^2): 2/0.625, 4/1.25, 8/2.5 mg

Medication	**Initial Dose for approved Indications in Adults (also see footnote b)**	**Usual or Target Maintenance Dose (Adults)**	**Clinical Benefit (Based on Level A evidence in adults)**	**How Supplied/Cost of 30-day supply (generic, if available)[a]**
Quinapril (*Accupril*, generics)	**HTN**: 10 to 20 mg once daily[b] **HF**: 5 mg BID[8,b]	**HTN**: 20 to 80 mg once daily (Canada: 20 to 40 mg once daily)(divide BID for better control) **HF**: 20 mg BID[8]	**HF**: improves symptoms and NYHA classification	5 (US), 10, 20, 40 mg US: ~$10 (40 mg once daily) Canada: ~$15 (40 mg once daily) **With HCT** (*Accuretic*; indicated for HTN only; not for initial therapy; not for volume-depleted patients [US]; not recommended if CrCl ≤30 mL/min): 10/12.5, 20/12.5, 20/25 mg
Ramipril (*Altace*, generics) Long duration of action.[30]	**HTN**: 2.5 mg once daily[b] **High CV risk**: 2.5 mg once daily **HF post-MI**: 1.25 to 2.5 mg BID[b] **HF (off-label)**: 1.25 to 2.5 mg once daily.[8] (Canada: 1.25 to 2.5 mg BID[30])[b]	**HTN**: 2.5 to 20 mg once daily (Canada: 2.5 to 10 mg once daily, max 20 mg once daily)(divide BID for better control)[b] **High CV risk**: 10 mg once daily **HF post-MI**: 5 mg BID[8,b] **HF (off-label)**: 10 mg once daily[8] (Canada: 5 mg BID[30])[b]	**High CV risk:** Reduce **mortality** (NNT = 45 patients for 5 years), **MI** (NNT = 42 patients for 5 years), and **stroke** (NNT = 67 patients for 5 years) in patients at high risk for cardiovascular events without LVD or heart failure. (~75% of study subjects had CAD).[26] **HF post-MI**: Reduce mortality in post-MI patients with heart failure (AIRE, NNT = 17 patients for 1.25 years).[27] **Nephropathy**: Reduce rate of **decline of GFR** in patients with non-diabetic kidney disease, as well as the risk of **doubling of serum creatinine** or **ESRD** (NNT = 4 patients for 1.3 years).[25]	1.25, 2.5, 5, 10 mg US: ~$10 (10 mg once daily) Canada: <$5 (10 mg once daily) **With HCT** (*Altace HCT* [Canada] indicated for HTN only; not for initial therapy; contraindicated if CrCl ≤30 mL/min): 2.5/12.5, 5/12.5, 5/25, 10/12.5, 10/25 mg

Medication	Initial Dose for approved Indications in Adults (also see footnote b)	Usual or Target Maintenance Dose (Adults)	Clinical Benefit (Based on Level A evidence in adults)	How Supplied/Cost of 30-day supply (generic, if available)[a]
Trandolapril (*Mavik* [Canada], generics)	**HTN**: 1 mg once daily **Post-MI with left ventricular dysfunction/failure**: 1 mg once daily.[8] **HF (off-label)**: 1 mg once daily[8] (Canada: 1 to 2 mg once daily[30])	**HTN**: 2 to 4 mg once daily (Canada: 1 to 2 mg once daily)(divide BID for better control)(little experience with doses >8 mg) **Post-MI with left ventricular dysfunction/failure**: 4 mg once daily. **HF (off-label)**: 4 mg once daily[8,30]	**Post-MI with left ventricular dysfunction/failure:** Reduces **mortality** (NNT = 14 patients for 2-4 years) and increases time to **progression to severe heart failure** in post-MI patients with left ventricular systolic dysfunction (NNT = 14 patients for 2-4 years).[28]	0.5 (Canada), 1, 2, 4 mg US: ~$14 (4 mg once daily) Canada: <$10 (4 mg once daily)

Abbreviations: ACEI = angiotensin-converting enzyme inhibitor; ARBs = angiotensin receptor blockers; BID = twice daily; BP = blood pressure; CAD = coronary artery disease; HF = heart failure; CrCl = creatinine clearance; CV = cardiovascular; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; ESRD = end stage renal disease; HCT = hydrochlorothiazide; HTN = hypertension; LVEF = left ventricular ejection fraction; LVH = left ventricular hypertrophy; MI = myocardial infarction; NNT = number needed to treat; NYHA = New York Heart Association Class; SCr = serum creatinine; RCT = randomized controlled trial; TID = three times daily

US product information used in preparation of this chart: *Lotensin* (January 2019), *Lotrel* (April 2021), *Lotensin HCT* (October 2020), captopril (Solco Healthcare, April 2023), captopril and hydrochlorothiazide (Rising, December 2022), *Vasotec* (December 2020), *Vaseretic* (September 2020), fosinopril (Chartwell Rx, May 2023), fosinopril and hydrochlorothiazide (Aurobindo, January 2022), *Zestril* (March 2020), *Qbrelis* (April 2023), *Zestoretic* (July 2021), moexipril (Glenmark, December 2015), perindopril (Aurobindo, January 2023), quinapril (Lupin, September 2020), quinapril and hydrochlorothiazide (Aurobindo, May 2022), *Altace* (June 2017), trandolapril (Aurobindo, February 2022).
Canadian product monographs used in preparation of this chart: benazepril (AA Pharma, December 2019), captopril (Teva, February 2021), *Vasotec* (June 2021), *Vaseretic* (November 2022), fosinopril (Sanis Health, December 2016), *Zestril* (July 2021), *Zestoretic* (March 2022), *Coversyl* (October 2022), *Coversyl Plus* (October 2022), *Accupril* (December 2022), *Accuretic* (December 2022), *Altace* (January 2021), *Altace HCT* (January 2023), *Mavik* (September 2019)

a. US cost is wholesale average cost (WAC). Pricing by Elsevier, accessed October 2023.
b. **Dosing of ACEI in special populations**: SCr 1 mg/dL = 90 umol/L

Benazepril:

- **kidney impairment** (eGFR <30 mL/min/1.73 m^2; Canada: CrCl <30 mL/min): initial 5 mg once daily. Max dose 40 mg/day if eGFR <30 mL/min/1.73 m^2.
- with a **diuretic**: initial 5 mg once daily.

Captopril

- kidney impairment: CrCl 10 to 50 mL/min, reduce total daily dose by 75% and divide BID; CrCl <10 mL/min., reduce dose by 50% and give once daily.[36] Hemodialysis, administer the daily dose after dialysis on dialysis days.[36]
- with a **diuretic**: start with doses of 6.25 to 12.5 mg (US)

Enalapril

- **geriatrics** (>65 years of age): initial 2.5 mg once daily (HTN)(Canada)
- **kidney impairment**: CrCl ≤30 mL/min, initial 2.5 mg once daily (HTN); SCr >1.6 mg/dL, initial 2.5 mg once daily (HF). Hemodialysis, based non-dialysis-days dose per clinical response, but give 2.5 mg on dialysis days, after dialysis.
- with a **diuretic**: initial 2.5 mg once daily (HTN)
- **hyponatremia** (sodium <130 mEq/L): initial 2.5 mg once daily (HF)

Fosinopril:

- **kidney impairment:** dose adjustment is not needed in hypertensive patients with kidney impairment, so consider cautious dosing in patients with kidney impairment switched from fosinopril to another ACE inhibitor. Lisinopril may provide better BP control than fosinopril at the same dose.[12]

Lisinopril:

- **Kidney impairment**: CrCl 10 to 30 mL/min, initial 2.5 mg (HF, post-MI) or 5 mg (HTN) once daily (US). Canada: initial 2.5 to 5 mg once daily (HTN). CrCl <10 mL/min or hemodialysis, initial 2.5 mg once daily. Max daily dose 40 mg once daily.
- With a **diuretic (HTN)**: 5 mg once daily.

Perindopril

- **Kidney impairment:** CrCl 30 to <60 mL/min, initial 2 mg once daily. Max dose 8 mg/day. CrCl <30 mL/min, not recommended (US). CrCl 15 to <30 mL/min, 2 mg every-other-day (Canada). Hemodialysis: 2 mg on dialysis days, after dialysis (Canada).

Quinapril

- **Geriatrics**: initial 10 mg once daily (HTN)
- **Kidney impairment**: CrCl 30 to 60 mL/min, initial 5 mg once daily. CrCl 10 to 29 mL/min, initial 2.5 mg once daily.[36] CrCl<10 mL/min, insufficient data for dosage recommendation.
- With a **diuretic**: initial 5 mg once daily (HTN)

Ramipril

- Canada

- **Kidney impairment (HTN)**: CrCl 10 to <40 mL/min/1.73 m^2 [SCr >2.5 mg/dL]): initial 1.25 mg once daily, max daily dose 5 mg. CrCl <10 mL/min/1.73 m^2, initial 1.25 mg once daily, max daily dose 2.5 mg.
- **Kidney impairment (HF post-MI)**: CrCl 20 to 50 mL/min/1.73 m^2, initial 1.25 mg once daily, max dose 1.25 mg BID.
- High CV risk: follow dosing for special populations as for other indications
- **Liver impairment**: max daily dose 2.5 mg
- With a **diuretic**: initial 1.25 mg
- **High CV risk**: follow dosing for special populations as for other indications.

- US
  - **Kidney impairment**: CrCl <40 mL/min, initial 1.25 mg once daily, max daily dose 5 mg (HTN, post-MI). In general, one-quarter (25%) of the usual dose of ramipril is expected to produce full therapeutic levels.
  - With a **diuretic, volume depletion**, or suspected **renal artery stenosis**: initial 1.25 mg once daily
  - Suspected **renal artery stenosis**: initial 1.25 mg once daily

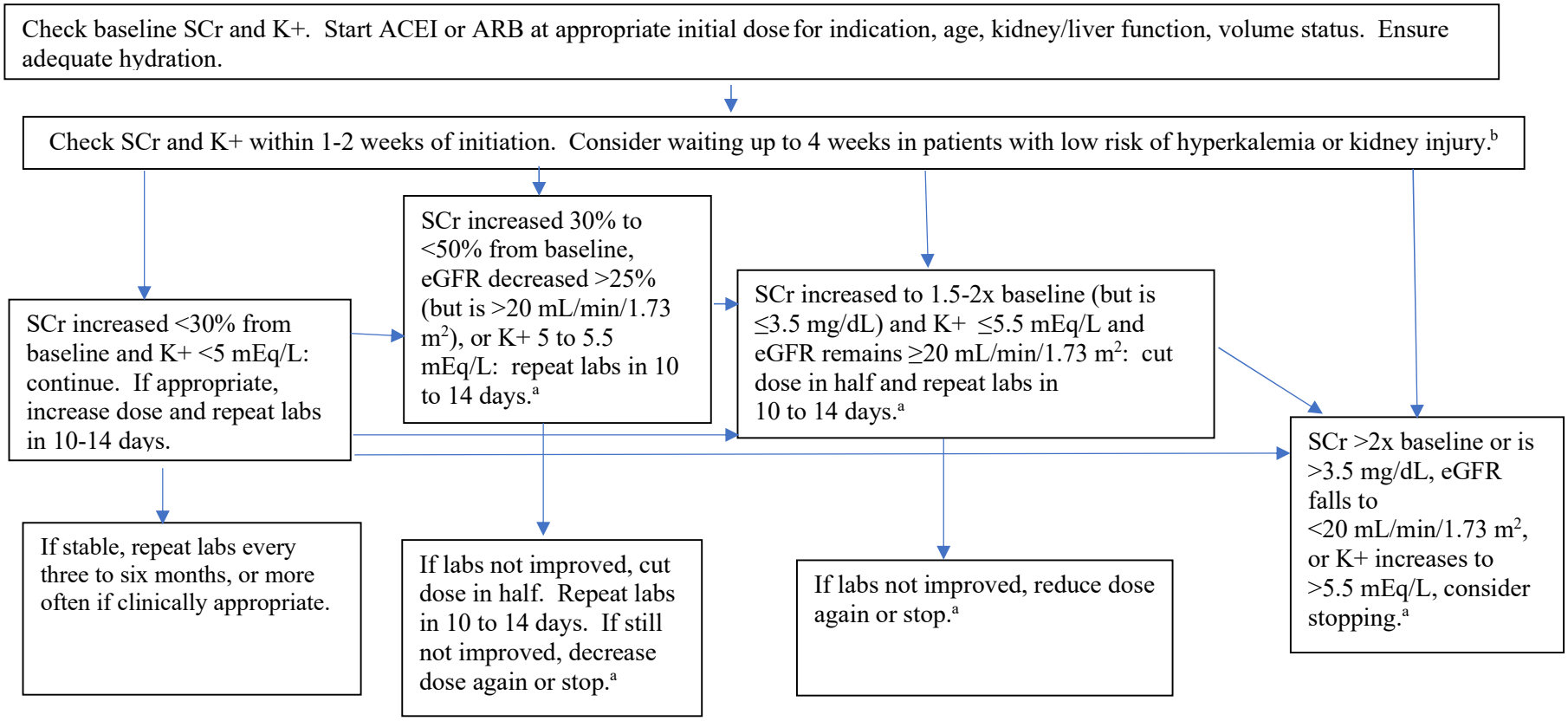
Trandolapril

- **Black patients**: 2 mg once daily (US)
- **Kidney impairment:** CrCl <30 mL/min (Canada: <30 mL/min/1.73 m^2), initial 0.5 mg once daily (Canada: max 1 mg once daily). CrCl <10 mL/min/1.73 m^2, max dose is 0.5 mg once daily (Canada).
- **Liver impairment (US: cirrhosis)**: 0.5 mg once daily
- With a **diuretic**: initial 0.5 mg once daily

--Continue to the next section for the *Monitoring ACEIs and ARBs* algorithm.—

Monitoring ACEIs and ARBs

—Algorithm based on references 4, 8, 30, 32-36 below. K+ = serum potassium; SCr = serum creatinine; SCr 1 mg/dL = 90 umol/L; K+ 5.5 mEq/L = 5.5 mmol/L.—



a. Ensure hydration; reassess diuretic use.[36] Consider stopping NSAIDs.[36] Provide dietary advice (e.g., moderate potassium intake, avoid salt substitutes).[35,36] For high K+ plus HTN or volume overload, consider a loop diuretic or thiazide, with or without oral sodium bicarbonate in patients with chronic kidney disease and metabolic acidosis.[36] If SCr increased >30% or eGFR decreased>25%, consider bilateral renal artery stenosis.[35] Consider rechallenge in 2-4 weeks.[33] Consider switching to trandolapril or fosinopril in the event of high K+.[4]

b. Risk factor examples: heart failure, impaired kidney function, high or borderline-high K+, history of hyperkalemia, history of kidney function deterioration on an ACEI or ARB, use of medications associated with hyperkalemia (e.g., spironolactone, eplerenone, trimethoprim, K+-sparing diuretics, NSAIDs, cyclosporine, digoxin), advanced age, low body mass index.[35,36]

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. 2004 Feb 1;69(3):548-56.
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Treatments for Rosacea

Rosacea is characterized by facial erythema, flushing, papulopustular lesions, thickened skin, and/or ocular involvement.[1] Therapeutic options include trigger avoidance (e.g., alcohol, spicy foods, sun exposure), appropriate skin care (e.g., gentle cleansers, mineral sunscreen), topical agents, oral therapies, and phototherapy.[2] This table reviews topical and oral options for the treatment of erythema and papulopustular lesions of rosacea.[c]

Topical Therapy[b]			
Drug[a]	**Pros**	**Cons**	**Comments**
Metronidazole 0.75%, 1%, (e.g., MetroGel, Noritate, generics [US]) **US**: ~$90/45 g **Canada**: $42/55 g (1%)	• Effective for papulopustular lesions.[1-3] • May be effective for erythema but little evidence in patients without papules/pustules.[1] • Safe in pregnancy.[4] • Well tolerated.[1]	• May cause mild itching, irritation, and dry skin.[3]	• First-line treatment of papulopustular lesions.[1,2] • May be better tolerated compared to azelaic acid.[3] • No difference in efficacy between 0.75% and 1% formulations.[1] • Improvement typically seen after three to six weeks.[3]
Azelaic acid (Azelex 20% [US], Finacea 15%, generics [US]) **US**: ~$145/50 g **Canada**: $45/50 g	• Effective for papulopustular lesions.[1-3,6] • Limited efficacy for erythema.[1] • Safe in pregnancy.[4]	• Can cause mild burning, stinging, and irritation.[3]	• First-line treatment of papulopustular lesions.[1,2] • As effective as metronidazole; however, may not be as well tolerated.[7] • Cream and foam cost over twice as much as the generic gel. • Less expensive 10% formulations are available OTC (many online); however, there is no evidence to support their efficacy. • Improvement typically seen after three to six weeks.[3]
Ivermectin 1% (Soolantra [US]; Rosiver [Canada], generic [US]) **US**: $475/45 g	• Effective for papulopustular lesions.[1,2,6,14] • Well tolerated.[1,8]	• May cause skin irritation, dryness, burning, and pruritus.[5,9] • More expensive compared to metronidazole and azelaic acid.	• First-line treatment of papulopustular lesions.[1,2] • May be slightly more effective than topical metronidazole 0.75%.[3,10] • Anti-inflammatory and antiparasitic (vs *Demodex* mites) effects.[2,11,d]

Topical Therapy[b]			
Drug[a]	**Pros**	**Cons**	**Comments**
Canada:$227/60 g			• May be better tolerated than azelaic acid.[12]
Minocycline 1.5% foam (Zilxi) (US only) **US**: $485/30 g	• Effective for moderate to severe papulopustular lesions.[13] • Well tolerated.[13] • Minimal systemic absorption.[13]	• Can cause pruritus.[13] • May temporarily tint skin yellow, but can be washed away about an hour after application.[13]	• May be considered if metronidazole or azelaic acid are not effective. • Formulation is flammable. Fire, flame, and smoking should be avoided during and immediately following application.[5]
Brimonidine gel 0.33% (Mirvaso [US], Onreltea [Canada], generic [US]) **US**: $520/30 g **Canada**:$142/30 g	• Effective for moderate to severe erythema.[1,2,8,9] • Well tolerated.[9]	• Not effective for reducing papulopustular lesions.[8] • Can worsen erythema and cause flushing or pruritus.[9] • Case reports of a rebound effect and worsening erythema after discontinuation.[1]	• Can be used as monotherapy for erythema.[1] • Similar in efficacy to oxymetazoline.[9] • Improvement may be seen within 30 minutes, with maximum effect at about three hours.[16] • Anecdotal reports of using (off-label) brimonidine 0.15% eye drops topically for rosacea.[17] May be a less expensive option.
Oxymetazoline 1% cream (Rhofade) (US only) **US**: $650/30g	• Effective for moderate to severe erythema.[2,9,22] • Well tolerated.[15]	• Not effective for reducing papulopustular lesions.[8] • May cause pruritus, redness, and worsening of inflammation or pustules.[5] • Less than 1% of patients report a rebound effect after discontinuation.[22]	• Can be used as monotherapy for erythema.[15] • Similar in efficacy to brimonidine.[9] • Oxymetazoline 0.05% nasal spray has been used topically for rosacea.[18] • Significantly reduces erythema within 1 hour; maintains effect for up to 12 hours.[15] • Appears to have lower rates of rebound effect and worsening erythema compared to brimonidine.[15]
Sodium sulfacetamide 10%/sulfur 5%	• Might be effective for papulopustular lesions and erythema.[6,19]	• Odor may be unappealing.[19] • Avoid in patients with sulfonamide allergies.[19]	• Off-label indication. • Limited evidence to support use.[6,8]
Benzoyl peroxide 5%/clindamycin 1%	• May reduce papulopustular lesions.[19]	• May trigger erythema, stinging with initial therapy.[4]	• Off-label indication. • Limited evidence to support use.[19]
Topical retinoids (tretinoin, adapalene)	• May reduce papulopustular lesions.[19]	• Use with caution due to risk of skin irritation, photosensitivity.[7,19] • May not be effective for erythema.[19] • Caution in pregnancy.[4]	• Off-label indication. • Limited evidence to support use.[2,6]

Topical Therapy[b]			
Drug[a]	**Pros**	**Cons**	**Comments**
Topical calcineurin inhibitors (pimecrolimus, tacrolimus)	• May improve erythema.[19]	• Reports of rosaceaform dermatitis when used for other indications.[19] • Do not appear effective for papulopustular lesions.[19]	• Off-label indication. • Limited evidence to support use.[6,8]
Permethrin 5% cream	• Effective in eliminating *Demodex* mites.[d] • May improve erythema and papulopustular lesions.[19]	• Long-term safety unknown.[19]	• Off-label indication. • Limited evidence to support use.[6,8,19]
OTC topical skin care products	• Ingredients often have claims of anti-inflammatory properties.[2]	• Little to no evidence to support claims of efficacy.[2]	• May include ingredients such as sulfur, allantoin, bisabolol, licorice root extracts, sallow bark, aloe vera, others.[2]

Oral Therapy[b]			
Drug	**Pros**	**Cons**	**Comments**
Antibiotics (doxycycline, minocycline, tetracycline, azithromycin, trimethoprim-sulfamethoxazole, erythromycin, metronidazole, clindamycin)	• Low-dose doxycycline is effective for papulopustular lesions.[1-3] • Generally inexpensive (exceptions doxycycline 40 mg, minocycline 40 mg [US only]) compared with other rosacea therapies. • Low-dose doxycycline has not been associated with antibiotic resistance.[2]	• Concerns about bacterial resistance (low-dose doxycycline may be an exception).[4] • Rosacea products (i.e., 40 mg doxycycline or minocycline) are more expensive than generic 50 mg forms and other antibiotics (e.g., tetracycline). ▪ 40 mg doxycycline:[a] **US**: ~$674/month, **Canada**: $88/month ▪ 40 mg minocycline:[a] **US**: $1,300/month • Various adverse drug reactions (e.g., gastrointestinal, photosensitivity).[1]	• Consider in patients who may prefer oral therapy or for moderate to severe disease.[1,6] • Low-dose (subantimicrobial dose) minocycline 40 mg (Emrosi [US only]) OR doxycycline 40 mg (Oracea [US], Apprilon [Canada]), all once daily, are approved for rosacea.[5,20,21] ▪ Approvals based on efficacy studies of 16 weeks duration.[5,20,21] ▪ Limited data suggest minocycline 40 mg once daily improves lesion count and treatment success in moderate to severe rosacea, compared to doxycycline 40 mg once daily.[23] ▪ Limited evidence with other antibiotics.[2] • Efficacy of low-dose doxycycline 40 mg is similar to 100 mg daily; however, the lower dose is better tolerated.[1,3] • Often used in combination with a topical product for short-term treatment of flares or as initial therapy (e.g., up to 12 weeks).[4]

Oral Therapy[b]			
Drug	**Pros**	**Cons**	**Comments**
Isotretinoin	• May be effective in combination with a topical agent for refractory cases of papulopustular lesions.[1,2]	• Contraindicated in pregnancy. • Requires monitoring for adverse effects (leukopenia, neutropenia, liver dysfunction, lipid abnormalities, etc).[1,5]	• Off-label indication. • Once rosacea is controlled, switch to intermittent therapy.[6]

a. Pricing based on the average wholesale acquisition cost (WAC) for generic formulation, if available. US medication pricing by Elsevier, accessed May 2025.

b. Topical monotherapy may be sufficient for mild disease. Multi-symptom (e.g., redness plus papules or pustules) or more severe disease may require a combination of treatments, especially for initial therapy.[2,8,19] After 8 to 12 weeks, if response is inadequate, an increased dose or frequency can be tried or an alternative agent used.[1] Once improvement is achieved, the dose can be tapered and/or the medication can be switched to a milder agent.[1] First-line treatments for mild rosacea are recommended for long-term maintenance therapy.[1]

c. Various meds are sometimes used off-label to control flushing in patients with rosacea including NSAIDs, antihistamines, clonidine, and beta-blockers.[2] Evidence of efficacy with these meds is limited.[2]

d. *Demodex* mites are part of normal skin flora; however, they are often found at higher concentrations in patients with rosacea compared to those without.[2] They appear to be a rosacea trigger for some patients.[1,6]

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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Comparison of Commonly Used Diuretics

full update May 2025

This chart reviews the indications, dosing, kinetics, cost, and place in therapy for commonly used diuretics.

NOTE: *Information based on US prescribing information unless otherwise noted. Indication and dosing information from Canadian labeling is provided if significantly different from US labeling.*

Diuretic/Availability	USUAL Adult Dose Range	Onset	Duration	Cost[a]	Comments
THIAZIDE DIURETICS are among the drugs that significantly increase blood glucose. They can also increase triglycerides and cholesterol minimally.[1] Other side effects include hypokalemia, metabolic alkalosis, hyponatremia, and hypomagnesemia.[1,2] Thiazides reduce urinary calcium excretion, an effect that may be beneficial to people at risk of osteoporosis or kidney stones.[1] Contrary to popular belief, thiazides, particularly metolazone, can be effective if CrCl is <30 mL/min.[6,7]					
Chlorothiazide (oral) (not available in Canada) Diuril 250 mg/5 mL, suspension	**Edema** 0.5-1 g QD to BID **HTN** 0.5-1 g QD or divided BID	≤2 hrs	6 to 12 hrs	US: 500 mg: ~$2.50 (brand)	•Brand only.
Chlorothiazide (IV) (not available in Canada) 500 mg injection (IV)	**Edema** 0.5-1 g QD to BID	15 min	N/A	US: 500 mg injection: ~$30	•Only thiazide available as an injectable.
Chlorthalidone HemiClor (US) 12.5 mg tabs Thalitone (US) 15 mg, 25 mg tabs 25, 50 mg tabs (US); 12.5, 25, 50 mg tabs (Canada)	**Edema** 50 to 200 mg QD or 100 to 200 mg every other day (Canada: 50 mg QD, max) **HTN** 12.5 to 100 mg QD (Canada: 25 to 50 mg QD)	~2.6 hrs	48 to 72 hrs	US: 25 mg tab: ~$0.40 Canada: 50 mg tab: ~$0.15	•Diuretic with most evidence for improved CV outcomes (e.g., used in ALLHAT).[1] Has not been proven to provide better cardiovascular outcomes than hydrochlorothiazide.[3] Comparative study ongoing.[4] •May be more effective in lowering SBP (by ~5 mmHg) over a full 24-hour period than hydrochlorothiazide.[5] •12.5 mg chlorthalidone ~ hydrochlorothiazide 25 mg.[1] •In combination products, only available with atenolol or azilsartan.

Diuretic/Availability	USUAL Adult Dose Range	Onset	Duration	Cost[a]	Comments
Hydrochlorothiazide 12.5, 25 mg, 50 mg tabs; 12.5 mg cap (US)	**Edema** 25 to 100 mg QD or divided (Canada: 25 to 100 mg QD or BID) **HTN** 12.5 QD to 50 mg QD or divided BID (Canada: 50 to 100 mg QD or divided)	≤2 hrs	6 to 12 hrs	US: 25 mg tab: ~$0.02 Canada: 25 mg tab: ~$0.02	•Most commonly prescribed thiazide.[1] •Most widely available diuretic in combination products with other antihypertensives.[1]
Indapamide 1.25, 2.5 mg tabs	**Edema** (US only) 2.5 to 5 mg QD **HTN** 1.25 to 2.5 mg QD	1 to 2 hrs[2]	At least 24 hrs[2]	US: 1.25 mg tab: ~$0.20 Canada: 1.25 mg tab: ~$0.15	•Reduced CV events (heart failure and death from stroke) in hypertensive patients ≥80 years vs placebo.[8] •May be more effective in lowering SBP (by ~5 mmHg) over a full 24-hour period than hydrochlorothiazide.[9] •In combo product with perindopril (Canada). •1.25 mg ~ hydrochlorothiazide 25 mg[9]
Metolazone Zaroxolyn (Canada) US: 2.5, 5, 10 mg tabs Canada: 2.5 mg tabs	**Edema** 5 to 20 mg QD **HTN** 2.5 to 5 mg QD	≤1 hr	≥24 hr (dose-dependent)	US: 2.5 mg tab: ~$0.45 Canada (brand): 2.5 mg tab: ~$0.25	•Absorption is slow and unpredictable.[10] •More effective than other thiazides at CrCl <30 mL/min.[10]
LOOP DIURETICS are more effective diuretics than thiazides, but lack outcomes data for hypertension.[1,11] They are best reserved for edematous conditions (e.g., heart failure, renal failure).[1] Loops are generally recommended over thiazides for patients with GFR <30 mL/min/1.73 m^2.[7] A thiazide can be added to a loop to enhance diuresis.[7] Like thiazides, loops can cause hypokalemia and metabolic alkalosis.[11] Loops are less likely to cause hyponatremia or hypomagnesemia.[11,12] Loops increase excretion of calcium, instead of reducing it like thiazides.[1] Loops can cause dose-dependent ototoxicity (furosemide >bumetanide).[13] **For edematous states, loops are usually dosed intermittently, as needed.**					
Bumetanide (oral) Bumex (US) Burinex (Canada) US: 0.5, 1, 2 mg tabs Canada: 1, 5 mg tabs	**Edema**: 0.5 to 2 mg QD. If needed, repeat every 4 to 5 hrs (max 10 mg/day).	0.5 to 1 hr	4 to 6 hrs (dose-dependent)	U.S.: 1 mg tab: ~$0.40 Canada (brand): 1 mg tab: ~$0.90	•Well-absorbed[13] •1 mg oral bumetanide = 40 mg oral furosemide[13] •Canadian labeling recommends a max dose of 5 mg in patients with hepatic failure.

Diuretic/Availability	USUAL Adult Dose Range	Onset	Duration	Cost[a]	Comments
Bumetanide (IV or IM) (not available in Canada) 0.25 mg/mL injection	**Edema** 0.5 to 1 mg. If needed, repeat every 2 to 3 hrs (max 10 mg/day).	IV: minutes IM: 40 min.[14]	3 to 6 hrs[14]	US: 1 mg injection: ~$0.65	•1:1 IV to PO conversion[13]
Ethacrynic acid (oral) Edecrin 25 mg tab	**Edema** 50 mg QD to 50 to 100 mg BID Take after a meal.	30 min	6 to 8 hr	US: 25 mg tab: ~$2.15 Canada (brand): 25 mg tab: $1.30	•Useful in patients resistant to other diuretics (Canada). •50 mg oral ethacrynic acid ~ 40 mg oral furosemide[15] •More ototoxic than other loops.[7] •Only loop without a sulfa group.[7] May be useful for patients with allergic reaction to other loops or thiazides. See our chart, *Sulfa Drugs and the Sulfa-Allergic Patient*, for more information.
Ethacrynate sodium (IV) Sodium Edecrin (US) 50 mg injection	**Edema** 50 mg x 1 (or 0.5 to 1 mg/kg; max 100 mg). May repeat (at a different site to avoid phlebitis) if needed.	5 min	2 hrs[14]	US: 50 mg: ~$1,900 Canada: 50 mg: $480	•Not for IM or subcutaneous injection. •More ototoxic than other loops.[7] •Only loop without a sulfa group.[7] May be useful for patients with allergic reaction to other loops or thiazides. See our chart, *Sulfa Drugs and the Sulfa-Allergic Patient*, for more information.
Furosemide (oral) Lasix 20, 40, 80 mg tabs; 10 mg/mL oral solution; 40 mg/5 mL oral solution (US); *Lasix Special** (Canada) *see comments section	**Edema** 20 to 80 mg (Canada: 40 to 80 mg). May repeat, or increase by 20 to 40 mg, in 6 to 8 hrs. (max 600 mg/day; Canada: 200 mg/day). When effective dose reached, give QD or divide BID (morning and early afternoon; Canada: may repeat one to three times daily) **HTN** 40 mg BID (Canada: 20 to 40 mg BID)	<1 hr	6 to 8 hr	US: 40 mg tab: ~$0.05 Canada: 40 mg tab: ~$0.04	•Loop with poorest oral absorption (~50% [range 10% to 100%].[13] •*Lasix Special** is a high-dose oral formulation (500 mg tab) of furosemide, for hospitalized patients with GFR 5 to 20 mL/min/1.73 m^2 not responding to usual furosemide doses. Initial dose is guided by the IV dose found to be effective. Or, in patients who do not respond adequately to 80 to 160 mg of oral furosemide, the initial dose is 250 mg. After 4 to 6 hrs, if response is inadequate, dose may be increased to 500 mg. Max daily dose 1,000 mg.

Diuretic/Availability	USUAL Adult Dose Range	Onset	Duration	Cost[a]	Comments
Furosemide (subcutaneous) (not available in Canada) Furoscix 8 mg/mL subcutaneous solution	**Edema** The single-dose infuser delivers 30 mg over the first hour, then 12.5 mg/hour for four hours (80 mg over 5 hrs).	Rapid[16]	≥8 hrs after initiation of dosing	US: ~$950	•Furoscix is a wearable patch pump with furosemide solution buffered to pH 7.4 to allow for subcutaneous administration.[16] •Similar diuretic efficacy to two doses of furosemide 40 mg IV two hours apart.[16]
Furosemide (IV or IM) 10 mg/mL injection	**Edema** 20 to 40 mg. May repeat, or increase by 20 mg, in 2 hrs. (Canada: max 100 mg/day). Once effective dose reached, give QD or divide BID. For **pulmonary edema**, dose is 40 mg, increased to 80 mg in 1 hr if needed (Canada: 40 mg, repeated in to 1.5 hrs if needed.)	IV: ≤5 min	IV: ~2 hr	US: 20 mg/2 mL vial: ~$1 Canada: 20 mg/2 mL amp: ~$1.30	•When switching to/from oral furosemide, keep in mind that oral furosemide bioavailability is ~50% (range 10% to 100%).[13] •Administer over one to two minutes (bolus) or as a continuous infusion at ≤4 mg/min).
Torsemide (not available in Canada) *Soaanz*, *Demadex* (brand discontinued) 5 mg, 10 mg, 20 mg, 40 mg (Soaanz), 60 mg (Soaanz), 100 mg tabs	**Edema** 10 to 20 mg QD (max 200 mg/day) **HTN** 5 to 10 mg QD	≤1 hr	6 to 8 hrs	10 mg tab: ~$0.45	•Bioavailability 80% to 100%.[13] •20 mg oral torsemide = 40 mg oral furosemide[13] •Cirrhosis: start with 5 to 10 mg QD. Doses >40 mg/day have not been studied in cirrhosis.
POTASSIUM-SPARING DIURETICS are usually weak antihypertensives, but they can be added to a thiazide to minimize hypokalemia risk.[1] The risk of hyperkalemia is increased in kidney impairment and/or with use of an ACE inhibitor or ARB.[14]					
Amiloride *Midamor* 5 mg tab	5 to 10 mg QD (max 20 mg) See comments for indications.	2 hr	~24 hrs	US: 5 mg tab: ~$0.2 Canada (brand): 5 mg tab: ~$0.40	•Weak antihypertensive and diuretic effects that are somewhat additive to those of thiazides. •Indications: adjunct to thiazide or loop diuretic in patients with heart failure or hypertension, to maintain potassium levels; edema associated with cirrhosis (Canada). Rarely used alone.

Diuretic/Availability	USUAL Adult Dose Range	Onset	Duration	Cost[a]	Comments
Eplerenone *Inspra* 25, 50 mg tabs	**HFrEF post-MI** 25 to 50 mg (target dose) QD **HTN** 50 mg QD or BID **Note**: HFrEF indication requires dose reduction if potassium level ≥5.5 mEq/mL. Max dose 25 mg QD (HF) or BID (HTN) with moderate CYP3A4 inhibitors.	Not available	Not available	U.S.: 50 mg tab: ~$1.10 Canada: 50 mg tab: ~$2.50	•Eplerenone is an aldosterone antagonist with less progesterone and androgen receptor antagonism than spironolactone.[10] •Option for resistant hypertension.[1] •Benefit in HFrEF (morbidity and mortality reduction) due to RAS suppression.[7] •Helps offset loop or thiazide diuretic-related potassium and magnesium losses.[17] •Do not use if K >5.5 mEq/L (Canada: >5 mmol/L) at initiation, CrCl ≤30 mL/min (<50 mL/min for HTN), or with strong CYP3A4 inhibitors.
Spironolactone tablets *Aldactone* 25, 50 (US only), 100 mg tabs	**Edema** 25 to 200 mg QD or divided (see comments regarding cirrhosis) **HTN** 25 to 100 mg QD or divided (Canada: 200 mg max). **HF** 25 to 50 mg QD. See comments. **Hypokalemia** (Canada) 25 to 100 mg/day **Primary hyperaldosteronism** See comments	Not available	2 to 3 days[14]	US: 50 mg tab: ~$0.25 Canada: 25 mg tab: ~$0.04	•Benefit in HFrEF (morbidity and mortality reduction) due to RAS suppression.[7] •Option for resistant hypertension.[1] •Helps offset loop or thiazide diuretic-related potassium and magnesium losses.[17] •Do not use in severe kidney impairment (Canada) or hyperkalemia. •**HF**: consider 25 mg every-other-day if eGFR 30 to 50 mL/min/1.73 m^2 or if hyperkalemia develops. •**Primary hyperaldosteronism treatment**: 100 to 400 mg/day pre-op, or lowest effective dose for maintenance. •**Primary hyperaldosteronism diagnosis** (Canada) 400 mg/day x 4 days (short test), or 3 to 4 weeks (long test) •**Cirrhosis:** consider a max of 100 mg or 400 mg for Na+/K+ ratio >1 or <1, respectively (Canada)
Spironlactone suspension *Carospir* *Continued…*	**Edema due to cirrhosis** 75 mg to 100 mg QD (initiate in hospital) **HTN** 20 to 75 mg QD or divided	Not available	2 to 3 days[14]	US: 20 mg ~$15	•**Dosing not equivalent to tablets**. •Benefit in HFrEF (morbidity and mortality reduction) due to RAS suppression.[7] •Option for resistant hypertension.[1] •Helps offset loop or thiazide diuretic-related potassium and magnesium losses.[17] •Do not use in hyperkalemia.

Diuretic/Availability	USUAL Adult Dose Range	Onset	Duration	Cost[a]	Comments
Spironolactone suspension, continued	**HF** 20 to 37.5 mg QD				•**HF**: reduce dose to 20 mg every-other-day if hyperkalemia occurs on 20 mg QD. Initiate with 10 mg QD if eGFR 30 to 50 mL/min/1.73m^2.
Triamterene *Dyrenium* 50, 100 mg cap (Only combo products are available in Canada.)	**Edema** 100 mg BID (max 300 mg/day) Take after meals.	2 to 4 hr	7 to 9 hr	US (brand): 50 mg cap: ~$15	•Weak antihypertensive effect.[1]

Product labeling used in above chart, unless otherwise noted: **US**: Diuril suspension (November 2021), chlorothiazide injection (September 2023), chlorthalidone (Rising, November 2024), HemiClor (March 2025), Thalitone (May 2021), hydrochlorothiazide tab (Leading, April 2024), hydrochlorothiazide cap (Rising, September 2024), indapamide (Rising, April 2023), metolazone (Alembic, May 2024), Bumex tablets (August 2018), bumetanide injection (Camber, March 2025), Edecrin (August 2020), Lasix (August 2018), furosemide oral solution (Hikma, October 2023), Furoscix (March 2025), furosemide injection (Hikma, March 2025), Soaanz (December 2021), torsemide (Chartwell, February 2024), amiloride (Endo, November 2024), Inspra (October 2021), Aldactone (September 2023), Carospir (August 2023), Dyrenium (December 2024); **Canada**: chlorthalidone (Apotex, March 2023), hydrochlorothiazide (Sanis Health, October 2024), indapamide (Mylan, October 2024), Zaroxolyn (January 2023), Burinex (July 2022), Edecrin (December 2020), ethacrynate sodium (SteriMax, February 2024), Lasix Special (October 2022), Lasix oral solution (September 2022), Pro-furosemide tablets (January 2022), furosemide injection (Marcan, November 2024), Midamor (August 2010), Inspra (July 2023), Aldactone (December 2022)

Abbreviations: ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BID = twice daily; CrCl = creatinine clearance; GFR = glomerular filtration rate; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; HTN = hypertension; IM = intramuscular; IV = intravenous; Na+/K+ = sodium/potassium; PO = oral; QD = once daily; RAS = renin-aldosterone system

a. Wholesale acquisition cost (US) per dose (unless otherwise specified), for generic if available, of dose specified. US medication pricing by Elsevier, accessed April 2025. Canadian cost is wholesale.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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Comparison of Insulins (United States)

Modified May 2025

This chart compares insulins in regard to onset, duration, and cost. It also provides information on route of administration, stability of in-use products at room temperature, and place in therapy. Other resources pertaining to insulin include our charts, *How to Switch Insulin Products* and *Tips to Improve Insulin Safety*.

--Information in this chart is from US product information[a] unless otherwise specified.--

Interactive Note: Roll over each gray bar containing an insulin type to view its specific footnote. (All footnote content is also provided on page 3.)

Insulin	Usual Frequency/Duration	Select Formulations/Cost[b] (See footnote g for maximum units/injection for pens)	Stability, in-use, room temp[e]
Rapid-acting insulin.[d] Appear clear and colorless.			
Admelog (insulin lispro)	Inject within 15 min before or immediately after a meal. Lasts 3 to 5 hours[2]	• $100/10 mL vial • $40/3 mL SoloStar pen[g] • $190/5 of 3 mL SoloStar pen[g]	Vial, pen: 28 days
Humalog (insulin lispro)	Inject within 15 min before or immediately after a meal. Lasts 3 to 5 hours.[2]	• $70 ($25*)/10 mL vial • $150/5 of 3 mL cartridge ($30 each) • $160*/5 of 3 mL 100 unit/mL KwikPen[g], KwikPen Junior[g] ($30* each), or Tempo[g] • $420/2 of 3 mL KwikPen[g] 200 unit/mL *Authorized generic available for 10 mL vial and 100 unit/mL KwikPen and KwikPen Junior.	Vial, cartridge, pen: 28 days
NovoLog (insulin aspart)	Inject within 5 to 10 min before a meal. Lasts 3 to 5 hours.	• $70/10 mL vial • $130/5 of 3 mL Penfill cartridge • $140/5 of 3 mL FlexPen[g]	Vial,cartridge, pen: 28 days
Merilog (insulin aspart-szjj)	Inject within 5 to 10 min before a meal. Lasts 3 to 5 hours.	• 10 mL vial[f] • 5 of 3 mL Solostar pen[f,g]	Vial, pen: 28 days
Apidra (insulin glulisine)	Inject within 15 min before a meal, or within 20 min after the start of the meal. Lasts 3 to 5 hours.[2]	• $90/10 mL vial • $160/5 of 3 mL SoloStar pen[g]	Vial, pen: 28 days
Fiasp (insulin aspart)	Inject at the start of the meal, or within 20 min after the start of the meal. Lasts 3 to 5 hours.[2]	• $290/10 mL vial • $560/5 of 3 mL FlexTouch pen[g] • $540/5 of 3 mL PenFill cartridge • $290/5 of 1.6 mL PumpCart cartridge	Vial, pen cartridge, pen: 28 days
Lyumjev (insulin lispro-aabc)	Inject within 20 minutes after the start of the meal. Lasts up to 5 hours.[6]	• $270/10 mL vial • $530/5 of 3 mL 100 unit/mL KwikPen[g] ($110 each) • $530/5 of 3 mL 100 unit/mL Tempo pen[g] • $420/2 of 3 mL KwikPen[g] 200 unit/mL ($210 each)	Vial, pen: 28 days
Short-acting (regular) insulin.[d] Appear clear and colorless.			
Humulin R 100 units/mL	Inject about 30 min before the meal. Lasts about 8 hours (longer in obese patients).	$45/10 mL vial	Vial: 31 days
Humulin R 500 units/mL	Inject about 30 min before the meal. Lasts 21 hours (mean).	• $1,500/20 mL vial • $570/2 of 3 mL KwikPen[g] ($290 each)	Vial: 40 days Pen: 28 days
Novolin R	Inject about 30 min before the meal. Lasts about 8 hours.	• $50/10 mL vial • $90/5 of 3 mL FlexPen[g] ($20 each)	Vial: 42 days Pen: 28 days

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Comparison of Insulins (United States)

Modified May 2025

Insulin	Usual Frequency/Duration	Select Formulations/Cost[b] (See footnote g for maximum units/injection for pens)	Stability, in-use, room temp[e]
Intermediate-acting (NPH) insulin.[d] Appear cloudy.			
Novolin N	Once or twice daily.[3] Lasts up to 24 hours.[2]	• $50/10 mL vial; $90/5 of 3 mL FlexPen[g] ($20 each)	Vial: 42 days Pen: 28 days
Humulin N	Once or twice daily.[3] Lasts up to 24 hours.[2]	• $45/10 mL vial • $140/5 of 3 mL KwikPen[g]($30 each)	Vial: 31 days Pen: 14 days
Long-acting insulin analogues.[d] Appear clear and colorless.			
Basaglar (insulin glargine)	Once daily at the same time each day. Lasts ~24 hours.	• $330/5 of 3 mL KwikPen[g] ($70 each) or Tempo[g] **Note**: Basaglar is **not** a generic for Lantus.	Pen: 28 days
Lantus (insulin glargine)	Once daily at the same time each day. Median duration 24 hours (range 10.8 to >24 hours; sampling period 24 hours).	• $60/10 mL vial • $100/5 of 3 mL SoloStar pen[g] ($20 each)	Vial, pen: 28 days
Rezvoglar (insulin glargine-aglr)[c]	See *Lantus*.	• $92/5 of 3mL KwikPen[g]	Pen: 28 days
Semglee (insulin glargine-yfgn)[c]	See *Lantus*.	• $270/10 mL vial • $400/5 of 3 mL pen[g]	Vial, pen: 28 days
Toujeo (insulin glargine) (300 units/mL)	Once daily at the same time each day. May take ≥5 days to see maximum effect. Lasts >24 hours.[8]	• $430/3 of 1.5 mL SoloStar pen[g] ($140 each) • $710/5 of 1.5 mL SoloStar pen[g]; $570/2 of 3 mL Max SoloStar pen[g] ($290 each)	Pen: 56 days
Ultra-Long-acting insulin.[d] Appears clear and colorless.			
Tresiba (insulin degludec)	Once daily at any time of day. Lasts at least 42 hours.	• $340 vial (100 units/mL) • $510/5 of 3 mL 100 units/mL FlexTouch pen[g] • $610/3 of 3 mL 200 unit/mL FlexTouch pen[g]	Vial, pen: 56 days
Insulin Mixes.[d] Appear cloudy.			
NovoLog Mix 70/30	Give within 15 min before, or after starting to eat (type 2 diabetes). Lasts up to 24 hours.	• $70/10 mL vial • $140/5 of 3 mL FlexPen[g]	Vial: 28 days Pen: 14 days
Humalog Mix 75/25	Give within 15 min before the meal. Mean duration about 23 hours (range: 18 to 24 hours).	• $90/10 mL vial • $160*/5 of 3 mL KwikPen[g] ($30* each) *Authorized generic available for KwikPen.	Vial: 28 days Pen: 10 days
Humalog Mix 50/50	Give within 15 min before the meal. Lasts at least 22 hours.	• $90/10 mL vial • $160/5 of 3 mL KwikPen[g] ($30 each)	Vial: 28 days Pen: 10 days
Humulin 70/30	Give about 30 to 45 min before the meal. Mean duration about 23 hours (range: 18 to 24 hours).	• $45/10 mL vial • $140/5 of 3 mL KwikPen[g] ($30 each)	Vial: 31 days Pen: 10 days
Novolin 70/30	Give about 30 min before the meal. Lasts up to 24 hours.	• $50/10 mL vial • $90/5 of 3 mL FlexPen[g] ($20 each)	Vial: 42 days Pen: 28 days

Comparison of Insulins (United States)

Modified May 2025

Footnotes

a. Prescribing information used in creation of this chart: Admelog (August 2023), Humalog (August 2023), NovoLog (February 2023), Merilog (February 2025), Apidra (November 2022), Fiasp (June 2023), Lyumjev (October 2022), Humulin R 100 units/mL (June 2023), Humulin R 500 units/mL (February 2024), Novolin R (November 2022), Novolin N (November 2022), Humulin N (March 2023), Basaglar (July 2021), Lantus (June 2023), Rezvoglar (August 2024), Semglee (March 2025), Toujeo (August 2024), Tresiba (July 2022), NovoLog Mix 70/30 (February 2023), Humalog Mix 75/25 (July 2023), Humalog Mix 50/50 (July 2023), Humulin 70/30 (December 2024), Novolin 70/30 (November 2022).

b. Wholesale acquisition cost (WAC), for generic if available. Medication pricing by Elsevier, accessed December 2024. Some products are also available in 3 mL vials (e.g., for institutional use). "Each" means pen or cartridge can be purchased individually.

c. Semglee (insulin glargine-yfgn) and Rezvoglar (insulin glargine-aglr): May substitute for Lantus in many states (interchangeable biosimilar).[5] See our *Facts About Biosimilars*.

d. **Rapid-acting analogues**: prandial human insulin analogues (rDNA origin). Onset 10 to 30 minutes (*Fiasp* and *Lyumjev* are faster. *Fiasp* is formulated with niacinamide and *Lyumjev* is formulated with treprostinil and citrate for faster absorption.)[2,6,7] For type 1 diabetes, recommended at each meal, plus one or two injections of basal insulin each day.[4] For type 2 diabetes, once daily at largest meal plus basal insulin, or basal-bolus regimen (i.e., two or three times daily with meals plus basal insulin).[3] All are given via subcutaneous injection. Humalog 100 unit/mL, Lyumjev, Fiasp, NovoLog, Apidra, and Admelog can be given subcutaneously via insulin pump. Fiasp, Humalog 100 unit/mL, Apidra, NovoLog, Admelog, and Lyumjev 100 unit/mL can be given by intravenous infusion.
Short-acting (regular): regular human insulin of rDNA origin. Available OTC (100 unit/mL only). Onset about 30 minutes (<15 min for the 500 unit/mL concentration). Longer time to onset and longer duration than rapid-acting analogues, but lag time between regular insulin administration and meals may not be needed for all patients with type 2 diabetes.[1] For type 1 diabetes, non-preferred alternative to rapid-acting insulin at each meal, with one or two injections of basal insulin each day.[4] For type 2 diabetes, once daily at largest meal plus basal insulin, or basal-bolus regimen (i.e., two or three times daily with meals plus basal insulin).[3] Can be given subcutaneously, or by intravenous infusion (100 unit/mL concentration only).
Intermediate-acting (NPH): human insulin (rDNA origin) isophane suspension. Available OTC. For type 1 diabetes, may be used as the basal component of basal-prandial regimens (analogues preferred).[4] An initial insulin option in type 2 diabetes, often as an add-on to oral agents.[3] As type 2 diabetes progresses, may be used with mealtime rapid- or short-acting insulin with the largest meal.[3] Onset 90 min.[2] Administered subcutaneously.
Long-acting: human insulin analogue (rDNA origin). For type 1 diabetes, preferred as the basal component of basal-prandial regimens.[4] An initial insulin option in type 2 diabetes, often as an add-on to oral agents.[3] As type 2 diabetes progresses, may be used with mealtime rapid- or short-acting insulin with the largest meal.[3] Administered subcutaneously.
Ultra-Long-acting: human insulin analogue (rDNA origin). Administered via subcutaneous injection. Consider for patients with severe or nocturnal hypoglycemia on another basal analogue, or with hypoglycemia risk factors,[9-11] or adherence problems.
Insulin Mixes: human insulin analogue (rDNA origin) solution and protamine-crystallized human insulin analogue suspension (NovoLog Mix 70/30, Humalog Mix 75/25, Humalog Mix 50/50). Others are human insulin (rDNA origin) solution and human insulin isophane suspension. Humulin 70/30 and Novolin 70/30 available OTC. Generally not appropriate for type 1 diabetes due to lack of dose flexibiltiy.[4] In type 2 diabetes, typically started after failure of basal insulin plus non-insulin.[3] Usually started pre-breakfast and pre-supper.[3] Administered subcutaneously.

e. Additional stability information: **Admelog**: pump reservoir 7 days; IV infusion 4 hours (0.1 to 1 unit/mL in NS); **Apidra**: pump reservoir 48 hours; IV infusion 48 hours (0.05 to 1 unit/mL in NS); **Fiasp**: pump cartridge 4 days; pump reservoir 6 days; IV infusion 24 hours (0.5 to 1 unit/mL in NS or D5W); **Humalog**: pump reservoir (Humalog 100 unit/mL) 7 days; IV infusion 48 hours (0.1 to 1 unit/mL in NS); **NovoLog**: pump reservoir 7 days; IV infusion 24 hours (0.05 to 1 unit/mL in NS, others); diluted 1:1 (U-50) or 1:9 (U-10) with Insulin Diluting Medium for NovoLog 28 days **Lyumjev**: pump reservoir 9 days; IV infusion 12 hours (1 unit/mL in NS or D5W); **Humulin R** 100 units/mL IV infusion: 48 hours (0.1 to 1 unit/mL in NS); **Novolin R**: IV infusion 24 hours (0.05 to 1 unit/mL in NS, D5W, D10 with KCl 40 mEq/L).

f. WAC unavailable at time of writing.

g. Maximum units/injection for pens:
- 30 units/dose: Humalog Junior KwikPen
- 60 units/dose: Humalog KwikPen (U-100, U-200), Humalog Tempo, Humalog Mix 50/50 KwikPen, Humalog Mix 75/25 KwikPen, Humulin N KwikPen, Humulin 70/30 KwikPen, Lyumjev KwikPen (U-100, U-200), Lyumjev Tempo, Novolin N FlexPen, Novolin R FlexPen, Novolin 70/30 FlexPen, Novolog FlexPen, Novolog Mix 70/30 FlexPen
- 80 units/dose: Admelog Solostar, Apidra Solostar, Basaglar KwikPen, Basaglar Tempo, Fiasp FlexTouch, Merilog Solostar, Lantus Solostar, Semglee pen, Toujeo Solostar, Tresiba FlexTouch (U-100)
- 160 units/dose: Tresiba FlexTouch (U-200), Toujeo Max Solostar
- 300 units/dose: Humulin U-500 KwikPen

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Emergency Epinephrine Devices

modified April 2025

In addition to the well-known *EpiPen*, there are several other emergency epinephrine devices to treat anaphlyaxis.[1,2,7] *Auvi-Q*'s (US) 0.1 mg auto-injector is marketed to have a lower risk of adverse effects (e.g., tremor, heart palpitations) in younger patients. It also has a smaller needle, designed to penetrate more often into muscle rather than bone in younger patients. *Emerade* (Canada) offers a 0.5 mg strength which is marketed as an option for heavier patients.[8] However, data are lacking to support the benefits of these newer strengths over the well-used 0.15 mg and 0.3 mg strengths. *Symjepi* (US) is a prefilled syringe that is proposed to be more intuitive than an autoinjector since patients see the needle and depress the plunger themselves.[37] *Neffy* (US) is a nasal spray which may be an option for some patients with a fear of needles. With high costs, shortages and recalls, generics, new strengths, a prefilled syringe, and a nasal spray; there are lots of questions about the different formulations and which one a patient should use. The choice between devices is determined by insurance coverage, availability, and ease of use. This document answers frequently asked questions about emergency epinephrine devices.

Note: Anaphylaxis is a potentially life-threatening condition. No matter which device is prescribed, all patients should be instructed on the appropriate, immediate use of their product. They should also be instructed to seek immediate medical attention (i.e., call 911) after epinephrine administration. Patients should always have two emergency epinephrine devices available in case a second dose is required during an anaphylactic reaction.

Question	Answer/Pertinent Information
Which emergency epinephrine devices are available? *Continued…*	Emergency epinephrine injection devices come in several strengths and are dispensed based on the patient's weight: • Most injection devices: 0.3 mg (30 kg and greater) and 0.15 mg (<30 kg). • *Auvi-Q* (US): also has 0.1 mg (7.5 kg to 15 kg). • *Emerade* (Canada): also has 0.5 mg (an option for adults >60 kg, based on clinical judgment).[41] Note that *Emerade* 0.15 mg strength has been approved but is not marketed at the time of publication. ***EpiPen*, *EpiPen Jr*:** The auto-injector is packaged in a tube-like carrier about five and a half inches long.[7] • Epinephrine injection, USP auto-injector (US; Mylan Specialty) is the authorized generic for *EpiPen*, *EpiPen Jr*.[19,32] • Epinephrine auto-injector (US; Teva Pharmaceuticals USA) is an AB-rated generic for *EpiPen* and *EpiPen Jr*.[9] ***Adrenaclick* (US)** is a cylindrical device, similar in length and size to the *EpiPen*.[7] • Epinephrine injection, USP auto-injector (US; Impax Generics) is the authorized generic for *Adrenaclick*.[27] ***Auvi-Q* (US), *Allerject* (Canada):** Credit card-sized (~3.5 x 2 inches) device with audio cues during administration.[5,7] ***Symjepi* (US)** is a prefilled syringe, about four inches in length.[29,37]

Question	Answer/Pertinent Information
Epinephrine devices, continued	***Emerade* (Canada)** is an auto-injector, packaged in a tubular protective case, similar in size to the *EpiPen*.[41] • Has a longer needle compared to other epinephrine injection devices. Promoted to more consistently deliver epinephrine intramuscularly rather than subcutaneously (i.e., through clothing and excess subcutaneous tissues).[42] • In May 2023, all *Emerade* auto-injectors were recalled due to risk of premature activation or of failure to activate. Date for return to market is unknown.[44] ***Neffy* (US)** is a one-dose **nasal spray** available as 2 mg (30 kg and more) and 1 mg (15 to 30 kg, 4 years and older).

Are there any alternatives to epinephrine injection devices?	**Epinephrine kits**: Vials or ampules of epinephrine in a kit with two doses, needles, and syringes.
	• May be considered as a **last resort** for someone in the community who is unable to afford injection devices.[18]
	• Cost for an assembled kit is estimated at ~$20.
	• May be a better option for institutions, clinics, etc (rather than patients) where clinicians are familiar with using syringes and needles.
	• May increase the risk for dosing errors and delay in treatment. Directions should be included in the kit with the dose and route of administration in bold print.
	• Filter needles may be needed if epinephrine ampules are used in the kit. Ensure you are providing the correct size needle for your patient with our chart, *Choosing the Correct Needle Size*.
	• For settings using epinephrine frequently, preparing syringes ahead of time may be helpful.
	  ◦ Pre-made syringes may be stable two to three months if protected from heat and light.[22,23]
	• Epinephrine should be given intramuscularly (rather than subcutaneously) for treatment of anaphylaxis for the fastest absorption.[28]
	• If dispensed to a patient in the community, patients must be:
	  ◦ reliable, trained, highly-motivated, and comfortable with the process.
	  ◦ able to accurately measure the dose and be trained to not use the entire vial.
	• Some emergency medical services (EMSs) are now stocking kits rather than *EpiPens*.[24]
	  ◦ reduces costs.
	  ◦ appears to increase appropriate use of epinephrine due to less hesitation about whether or not a reaction is serious enough to use a more costly epinephrine injection device.
	• *epinephrinesnap*, *epinephrinesnap-EMS*, and *epinephrinesnap-v* (US only).[25]
	  ◦ commercial kits available for healthcare professionals.
	  ◦ contains a vial of epinephrine 1 mg/mL, needles, syringes, alcohol pads, labels, and instructions.
	  ◦ training kits are also available.
	  ◦ cost is ~$90.

Question	Answer/Pertinent Information
What are some of the new products on the horizon?	Alternate modes of epinephrine administration (i.e., sublingual) are being studied:[43] • Clinical data is still lacking for most formulations, especially in pediatric patients and comparison studies.
Are epinephrine injection devices interchangeable?	**US**: • Teva's epinephrine auto-injector is AB-rated to *EpiPen* and *EpiPen Jr.*, and is interchangeable.[26] • *Adrenaclick* and *Auvi-Q* epinephrine injection devices have a therapeutic equivalence rating of BX (i.e., data are insufficient to determine therapeutic equivalence).[9] • Some states may allow interchanges of these products as governed by their state law.[10] • Two of the generic formulations, "epinephrine injection, USP auto-injector," (Mylan and Impax Generics) are authorized generics of *EpiPen* and *Adrenaclick*, respectively. This means that *EpiPen* and *Adrenaclick* have been relabeled and marketed under the generic product name. These generic products are identical to their respective brand name products. However, their automatic substitution is determined by individual state law.[11] • *Symjepi* is not interchangeable with the other epinephrine injection devices. **Canada**: • Follow provincial and territorial laws; *EpiPen*, *Allerject*, and *Emerade* are not usually interchangeable. One small pharmacokinetic study compared *EpiPen* to *Auvi-Q* in 69 healthy people. They demonstrated bioequivalence between these two products.[12]
What is the cost of each epinephrine device? ***Continued…***	Cost for packages of **two** devices:[a] • *EpiPen* or *EpiPen Jr.*: $610 ($190 in Canada) • *Auvi-Q* (US): $620 • *Allerject* or *Allerject Jr.* (Canada): $205 • *Adrenaclick* (US): $460 • *Adrenaclick* authorized generic epinephrine auto-injector, USP (US): $300 • *EpiPen* authorized generic epinephrine auto-injector, USP (US): $300 • Epinephrine auto-injector (US; Teva): $300 • *Symjepi* (US): $250 • *Emerade* (Canada): $175 • *Neffy* (US): $710 **NOTE**: Pricing between products varies based on discounts from individual pharmacies, insurance plans, and manufacturers. Reduced and $0 **co-pay cards** are available from most US manufacturers, for example (all information below is subject to change):

Question	Answer/Pertinent Information
Cost of epinephrine devices, continued	• An *EpiPen* $300 savings card (US only) for out-of-pocket costs is available for eligible patients. This online card (https://www.activatethecard.com/viatrisadvocate/epipen/welcome.html) can be printed or stored on a smartphone for presentation at a pharmacy. They also offer a Patient Assistance Program (for low income families) and an *EpiPen4Schools* program (for eligible schools) for *EpiPen* and its authorized generic (https://www.epipen.com/paying-for-epipen-and-generic). • *EpiPen*'s authorized generic epinephrine auto-injector (US only) offers a $25 off savings card to eligible patients, available online (https://www.activatethecard.com/mylanadvocate/mygenericeai/welcome.html). • *Adrenaclick*'s authorized generic epinephrine auto-injector (US only) offers a $0 co-pay coupon for patients with insurance and a $10 off savings coupon for cash paying customers. Their online card can be printed, then taken to the pharmacy or mailed for the rebate (https://sservices.trialcard.com/Coupon/Epinephrine). • *Auvi-Q* (US only) offers $35 co-pay for commercially insured patients. They also offer a Patient Assistance Program which offers *Auvi-Q* free of charge for eligible patients (https://www.auvi-q.com/get-auvi-q). • Generic epinephrine (Teva, US only) offers a $30 savings card to eligible patients (https://www.tevaepinephrine.com/globalassets/epipen/pdfs/tg-43298_epinephrine-injection-usp-auto-injectors-digital-copay-card---2023-update_final.pdf). • *Symjepi* (US only) offers copay support ($0 for eligible patients) and up to $100 off for cash paying customers (https://portal.trialcard.com/usworldmeds/symjepi/). • *Neffy* (US only) offers a co-pay savings program (as low as $25 if eligible) and a patient assistance program ($0 for eligible patients) (https://www.neffy.com/savings-and-support/)
What is the role for training devices? *Continued…*	Epinephrine devices are often used incorrectly, even by healthcare professionals.[5,14,15] • Each epinephrine device has a different administration technique so the instructions for proper use vary.[10] • Patients must be trained and educated on the use of their device. Repeat with every prescription filled/refilled.[10,14] • Ask your patients if they have had training on a device and try to dispense the same device if possible.[10] • Be sure that the patient understands if their device has changed and has new administration instructions. • For interchanged or new devices, patients must be retrained. Patients **must** be trained on correct administration technique.[5] • Demonstrate with a training device when available and then have the patient practice. • Training devices resemble the actual device but do not contain medication or a needle (for injectables). • Training devices can be used more than once so that patients, parents, and caregivers can all repeatedly practice proper administration. • Consider ordering training devices to have on hand in your pharmacy or office for teaching purposes.

Question	Answer/Pertinent Information
Training devices, continued	A training device is included with each *EpiPen* and its generic product two pack.[3,19] Additional trainers can be obtained by calling 800-395-3376. *Adrenaclick* and its generic product don't come with a training device, but training devices are available. They can be ordered online at http://epinephrineautoinject.com/order-product-trainers/, by calling 855-EPINEPH, or by mailing the form found inside the device package.[6] A training device is included with each *Auvi-Q* two pack. Additional trainers are available at www.auvi-q.com.[16] Free training devices are available for *Allerject* (www.allerject.ca) and *Emerade* (www.emerade.ca). **NOTE**: Training devices are only available for epinephrine **auto-injectors**, not for the *Symjepi* prefilled syringe. *Neffy* (US) does not come with a training device, but training devices are available. They can be ordered online at https://www.neffypro.com/#sign-up.

How do epinephrine injection devices differ?	Safety caps:
	• The *EpiPen,* its authorized generic, and the Teva generic auto-injectors all have one blue safety cap to remove at the non-needle end of the device.[3,19,38]
	• *Auvi-Q* and *Allerject* have a red safety guard to remove prior to use.[16,36]
	• The *Adrenaclick* and its generic have one blue cap at each end to remove prior to use.[6,31]
	• *Symjepi* has a blue cap that must be pulled off to expose the needle prior to use.[29]
	• *Emerade* has a needle cap/shield that must be removed prior to use.[41]
	
	Epinephrine injection devices are recommended to be given into the **outer thigh** for fastest absorption.
	• Consider the length of time the device must be held in place on the thigh when choosing, particularly for children:
	  • *EpiPen*, its authorized generic, and the Teva generic's recommended motion is to "swing and push," then hold in place for **three seconds**.[3,17,19,30,38]
	  • *Auvi-Q* is recommended to be pressed firmly and held in place for **two seconds**.[16]
	  • *Allerject* is recommended to be pressed firmly and held in place for **five seconds**.[36]
	  • *Adrenaclick* and its generic are recommended to be pressed and held firmly in place for **ten seconds**.[6,31]
	  • *Symjepi* should be injected downwards into the thigh while the patient is sitting. Once the needle is inserted, the plunger should be pushed down until it clicks and then held in place for **two seconds**.[29]
	  • *Emerade* should be pressed firmly, then held in place for **five seconds**.[41]

Question	Answer/Pertinent Information
How is emergency epinephrine nasal spray (*Neffy*) used?	Epinephrine nasal spray (*Neffy*) is for single use, with the entire dose administered upon activation.[46] • Device is ready to use once removed from packaging. • Either nostril can be used for administration. If a second dose is necessary, after five minutes, a new spray should be administered into the same nostril as the initial dose.[46] • Nasal device should not be primed or tested as this will discharge the dose. • Can be administered to a patient in any position (sitting, standing, lying down).
What is the shelf life of epinephrine devices?	The usual expiration date for epinephrine **injection** devices is 15 to 20 months from date of manufacture. *Neffy* **nasal** spray has a usual expiration of 30 months from date of manufacture and appears to be more stable to extreme heat exposure compared to *EpiPen* and *Symjepi*.[45,47] • Good inventory control can help ensure most patients have about a year (or more) before their next refill. • Patients should check the expiration date of their device to know when they'll need a refill. Some devices have a window to see the solution. If the solution is discolored or contains particles, the device should be replaced (regardless of the expiration date). • Many pharmacies, as well as the *EpiPen* website, offer refill reminders. Many of these devices expire before a patient needs to use them. • In response to previous decreased supplies of epinephrine auto-injectors and based on new stability data, the FDA authorized an extension of the expiration date of some specific lots of the **0.3 mg** *EpiPen* and its authorized generic by four months.[34] • For all other epinephrine injection devices not included in the FDA's expiration date extension, recently expired devices may lose some of their potency and shouldn't be relied on to treat a reaction. • If a patient is having an anaphylactic reaction, it may be preferable to use a recently expired device rather than not give any epinephrine at all.[13,21] Encourage patients to store their epinephrine devices properly. One small pilot study of the injections suggests that epinephrine concentrations may be reduced by up to 14% when the devices are left in a car's glovebox for 12 hours on a hot day.[39]

Question	Answer/Pertinent Information
Are there risks associated with use of emergency epinephrine devices?	There are no contraindications to the use of emergency epinephrine devices.[20,29] Accidental self-injection with these devices is not uncommon. • The device is sometimes held the wrong way, causing the thumb to be punctured rather than the thigh.[15] • *Auvi-Q* and *Allerject* are designed so the needle end is more easily identified, making them less likely to be held incorrectly.[17] • Patients can see the needle with *Symjepi*, which may make it less likely to be held incorrectly. • *Emerade* has an obvious opening at the needle end where the sheath is removed, and none on the opposite end.[41] There are reports of lacerations and embedded needles caused by epinephrine auto-injector use and misuse, mainly in children.[1] Needle exposure once administration is complete: • After use, the *EpiPen*, its authorized generic, and the Teva generic's orange tip extends to cover the needle.[3,19,38] • *Auvi-Q* and *Allerject* have a retractable needle system and safety tab mechanism located on the same end as the needle.[5] • The needle remains exposed on the *Adrenaclick* and its generic.[6,31] The device should be put back into the carrying case, needle first.[6,31] • After use, the needle of the *Symjepi* prefilled syringe should be covered by sliding the safety guard over the needle until it clicks.[29] • After use, a protective sheath covers the needle of the *Emerade* auto-injector.[41] There have been reports of the auto-injector labels sticking to the carrier tubes of the *EpiPen*, *EpiPen Jr*, and their authorized generics. This could cause a delay in the administration of the auto-injector. Pharmacists and patients should make sure auto-injectors can be easily removed from their outer tubes prior to dispensing and prior to when they need to use them, respectively.[40]

a. Pricing is wholesale acquisition cost (WAC). US medication pricing by Elsevier, accessed January 2024 (April 2025 for *Neffy*).

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69:548-56. https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

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Facts About Biosimilars

Full update November 2024

Numerous biosimilars are available in the US and Canada, and the list is growing. The differences between biosimilars, biologics, interchangeable products, and generics, as well as their various approval processes, can be confusing. Biosimilars may be preferred by payers as they are less costly than the reference product (but still expensive). This FAQ addresses questions that may come up regarding biosimilars, including interchangeability.

Question	Answer/Pertinent Information

What are biological products (biologic drugs) and biosimilars?	• **Biological products** (Canada: biologic drugs) are usually large complex molecules manufactured in living material (e.g., animal, plant, microorganism) using biotechnology methods.[2,21] They are much larger and more complex molecules or mixture of molecules than a traditional drug.[9]
	  ○ Examples include monoclonal antibodies (e.g., adalimumab), interferons and other cytokines, growth factors (e.g., filgrastim), thrombolytics and other enzymes, and immunomodulators.
	  ○ In the US, in 2020, several hormones (e.g., insulin, human growth hormone), which had historically been FDA-approved as drugs, were reclassified as biologics, allowing for the development of biosimilars and interchangeable products for these meds.[7]
	• **Biosimilars** are biological products (Canada: biologic drugs) that have been shown to be highly similar to an approved biological product (Canada: biologic drug), known as the **reference product** (Canada: reference biologic drug).[13,22]
	  • In Canada, biosimilars were previously referred to as subsequent entry biologics (SEBs).[22]

How do biosimilars receive approval?
 	
Continued…
	• Biosimilars are approved through an abbreviated pathway (in the US, created via the Biologics Price Competition and Innovation Act), that relies on existing safety and efficacy data of the reference product (Canada: reference biologic drug).[1,12,22]
	• Biosimilarity must be demonstrated between the reference product and the proposed biosimilar.[1,22]
	• The proposed biosimilar product does not need to independently establish safety and effectiveness.[1,22]
	• A biosimilar product can only be approved:
	  ○ if it has the same dosage form, route of administration, strength, and mechanism (for the desired indication[s]) as the reference product.[13,22] (US: minor differences in clinically inactive components [e.g., stabilizers, buffers] between the biosimilar and reference product are allowed.[2,22])
	  ○ for the condition(s) of use that have been approved for the reference product.[13,22] (Note that the biosimilar can have fewer indications and routes of administration than the reference product).[14,22]

Question	Answer/Pertinent Information
How biosimilars are approved, continued	• The manufacturer's application for a biosimilar must include, among other things, information demonstrating no clinically meaningful differences from the reference product in regard to safety, efficacy, potency, and purity based upon data from:[1,22] o analytical studies demonstrating that the biological product is "highly similar" to the reference product (US: except for minor differences in clinically inactive components).[1,22] o animal studies, if necessary.[1,22] o one or more clinical studies that demonstrates safety, purity, and potency in one or more indications for which the reference product is licensed. This usually includes assessment of immunogenicity, pharmacokinetics, and sometimes pharmacodynamics, and may include a comparative clinical trial.[1,22] ▪ An efficacy study is not required if there is sufficient information to support extrapolation of efficacy data from the reference product to the biosimilar.[1,22] ▪ In Canada, manufacturers must include a Risk Management Plan which explains how immunogenicity and other safety signals will be monitored post-marketing.[21] Biosimilar manufacturers must also keep abreast of post-marketing safety information for the reference biologic drug.[21] • In the US, there are additional requirements for **interchangeable** biologics, described later in this FAQ. • The majority of the product labeling for the biosimilar (dosing, administration, and warnings) will be the same as the reference biologic drug.[14,21] However, the biosimilar may be approved for fewer indications than the reference biologic drug and labeling will reflect this difference.[14,16,21] • Biosimilars cannot enter the market until the reference biologic drug patents for the desired indication(s) have expired or been litigated.[9,21]
In the **US**, can more than one biologic with the same active ingredient be approved via the new drug pathway?	• Multiple biologics with the same active ingredient can each be approved as **new drugs** (not as biosimilars) via the biologics license application (BLA) pathway, for example: o *Granix*, *Neupogen*, *Nivestym*, *Nypozi*, *Releuko*, and *Zarxio* are all filgrastim products. But *Granix* is **not** biosimilar to *Neupogen* (reference product).[19] Instead, *Granix* was approved through the traditional FDA approval pathway for a biologic drug (not the biosimilar pathway).[10] o There are multiple insulin glargine formulations on the market. *Basaglar* was approved after *Lantus*; however, it was approved as a **new biologic**, not as a biosimilar to *Lantus*.[19]
How does a biosimilar differ from a generic? *Continued…*	• Biosimilars are not generics. Biosimilars and generics are approved through different abbreviated pathways.[2] • Generic drugs are almost identical to the brand name drug. Small-molecule ("traditional") drugs are made through a predictable set of chemical reactions. However, biologics are made using manufacturing processes (e.g., cell production, purification processes) and living organisms (e.g., cell lines) that are unique to each manufacturer, making it impossible to make an exact copy of a biologic.[11] • FDA-approved generic drugs must contain the same active ingredient(s) as the brand-name/innovator drug (inactive ingredients may vary), be identical in strength, dosage form, and route of administration, have the same indications, and be bioequivalent (i.e., work in the same way and provide the same clinical benefit).[6]

Question	Answer/Pertinent Information
Biosimilar vs generic, continued	• **In the US**, in some cases, biologics may be approved through the generic drug approval pathway. • For example, glatiramer is a peptide, a specific type of biological product. The FDA has tools and guidance to facilitate evaluations of proposed generic peptides.[17] For example, *Glatopa* is a **generic** version of *Copaxone* (glatiramer); it is **not** a biosimilar of *Copaxone*. *Glatopa* was approved as a generic via the abbreviated new drug application (ANDA) pathway.[20] These products are therapeutic equivalents and may be substituted per the generic substitution regulations in your state.[18]

Are biosimilars interchangeable with the reference product/reference biologic drug?	• Biosimilars do not fall under the same rules for generic substitution as traditional drugs.
	United States
	• An **interchangeable** biologic is biosimilar to an FDA-approved reference product **and** meets additional standards for interchangeability.[1] Therefore, not all biosimilars are interchangeable. (See next section for info on identifying interchangeable biologics.)
	• Federal regulations allow an **interchangeable** biologic to be substituted for the reference product by a pharmacist without the intervention of the prescriber.[2] However, state pharmacy boards may have different regulations.[8,18]
	• To be **interchangeable**, an FDA-approved biosimilar must also prove that:[1]
	  o the proposed interchangeable biological product is expected to produce the same **clinical result** as the reference product in any given patient, (for example, *Semglee* [insulin glargine-yfgn] is an interchangeable biosimilar. *Semglee* has shown similar A1c lowering at six months compared to *Lantus*), **and**
	  o for a product that will be administered more than once to an individual, the risk in regard to safety or diminished effectiveness of switching between use of the proposed interchangeable product and the reference product is not greater than the risk of using the reference product without switching between products.
	Canada
	• Each province and territory in Canada determines the interchangeability of biosimilars, not Health Canada.[21]

How do you find out if a biosimilar and reference product/reference biologic drug are interchangeable?	**United States** • **The Purple Book** (https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/purple-book-lists-licensed-biological-products-reference-product-exclusivity-and-biosimilarity-or) enables the user to see if a biological product has been determined by the FDA to be interchangeable with the reference biologic.[4] • Biosimilar and interchangeable biologics licensed under section 351(k) of the Public Health Service Act are listed under the reference product to which biosimilarity or interchangeability was demonstrated.[4] **Canada** • Drugs designated as interchangeable may be denoted as such on your provincial Drug Benefit List.[5]

Question	Answer/Pertinent Information
How are biosimilars named?	**United States** • The FDA's naming convention for all biological products is a "core name" followed by an FDA-designated suffix composed of four lowercase letters attached to the core name with a hyphen.[3] Most of the suffixes are nonsensical.[3] o For example, *Nivestym* is named filgrastim-aafi. • The suffix format applies to originator biological products as well as biosimilars. Products without suffixes, or with suffixes that do not comply with the guidance, will receive new suffixes over time. The FDA is continuing to consider the appropriate suffix format for interchangeable products.[3] **Canada** • Biologic drugs should be identified by both their brand name and their non-proprietary or common name (e.g., "filgrastim [*Grastofil*]"). Each biologic drug has its own Drug Identification Number (DIN). Unlike in the US, a suffix is not used.[15]

What are some practical prescribing and dispensing implications for biosimilars?	• Review the prescribing information to determine the biosimilar's approved indications.[16]
	  o A biosimilar may have **fewer** indications and routes approved than the reference product.[13,14,21] This could happen if the reference product has an unexpired patent(s) on an indication, the biosimilar manufacturer only applies for certain indications, or the FDA/Health Canada does not allow the indication after reviewing the submitted data.[1,21]
	• Check carefully for important differences between biosimilars and the reference product (US)/reference biologic drug (Canada). There may be differences in **storage** requirements; shelf life; available dosages, strengths or concentrations; or inactive ingredients (e.g., **latex**, citrate).
	• **In the US**, interchangeable biosimilars may be substituted by the pharmacist without the intervention of the prescriber (depending on state law).[8,18] (This is analogous to substitution by the pharmacist of an A-rated generic.)
	• If a specific biologic brand is desired, prescribers can write for that particular brand (e.g., *Neupogen*) and specify "dispense as written" or "brand medically necessary," depending on state law.[18]
	• For noninterchangeable products, prescribers should specify the biosimilar's unique name to ensure the desired product is dispensed. For example, if *Zarxio* is desired, write the brand name or specific nonproprietary name (US only [e.g., filgrastim-sndz]) instead of just "filgrastim." Be aware that:
	  o in the hospital setting, a formulary-directed substitution might be made.
	  o coverage through a third-party payer/provincial plan may not be available for that brand.
	• Pharmacists should be aware of state/provincial laws on dispensing biosimilars. Some states may require the prescriber and/or patient to be notified if a substitution is made at the pharmacy.[18] Details of individual state regulations around biosimilar interchangeability can be found at https://www.cardinalhealth.com/en/product-solutions/pharmaceutical-products/biosimilars/state-regulations-for-biosimilar.html.
	• Keep in mind that patients enrolled in patient assistance programs for a reference biologic will need a new enrollment if they are switching to a biosimilar.
	• Ensure patient med lists accurately reflect the specific biosimilar that they are using (e.g., the brand name, suffix [US]).

Question	Answer/Pertinent Information
Should patients stick with the same biologic?	• An **interchangeable** biological product can be expected to produce the same **clinical result** as the reference product in any given patient.[5,8,16,21] o Designated **interchangeable** biological products (US) must show that (for products administered more than once to an individual) the risk in regard to safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.[1] • Reassure patients that it is ok to start or switch to a biosimilar. Even a biosimilar that is not designated as interchangeable is highly similar to, and has no clinically meaningful differences from, the reference product.[5]

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69:548-56. https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

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