BETA-ADRENERGIC RECEPTOR BLOCKING AGENTS

Generic Name	**Acebutolol**	**Atenolol**	**Bisoprolol**	**Carvedilol**	**Esmolol IV**
Trade Name	SECTRAL, generics	TENORMIN, generics	MONOCOR, generics	generics	BREVIBLOC
Dosage Forms	100 mg, 200 mg, 400 mg tablet	25 mg, 50 mg, 100 mg tablet	5 mg, 10 mg tablet	3.125 mg, 6.25 mg, 12.5 mg, 25 mg tablet	IV
Cardioselective	+	+	+	0	+
Partial Agonist/ISA*	+	0	0	0	0
Lipid Soluble	moderate	low	low-moderate	high	high
Dosing (usual)					
initial	100-200 mg bid	25-50 mg daily	2.5 mg daily	3.125-6.25 mg bid	Please see UHN IV drug list for dosing guidelines and prescribing restrictions Usual loading dose is 500 mcg/kg/min over 1 minute (by MD only) Usual infusion dose range for continuous infusion: 50-200 mcg/kg/min titrated to target mean arterial pressure (MAP) or systolic blood pressure (SBP) or heart rate (HR) parameter set by the prescribing MD (dependent on indication)
maximum	1200 mg/day (given once daily or bid)	200 mg daily	20 mg daily	25-50 mg bid	
Dosing in CHF	N/A	N/A			N/A
initial			1.25-2.5 mg daily	3.125 mg bid	
target			10 mg daily	25 mg bid	

BETA-ADRENERGIC RECEPTOR BLOCKING AGENTS

Generic Name	**Acebutolol**	**Atenolol**	**Bisoprolol**	**Carvedilol**	**Esmolol IV**
Bioavailability	40%	50-60% ↓ with food	80%	25-35% food slows rate of absorption and orthostatic side effects	100%
*** ISA** = intrinsic sympathomimetic activity					
Onset	1.5 hours	1 hour	2-4 hours	1 hour	Seconds to a minute
Peak	3 hours	3-6 hours	3-4 hours	1.5 hours	5 minutes
Metabolism	Liver	Minimal hepatic metabolism	Liver 50%	Liver (extensive)	Esterases in RBC cytosol
Active Metabolite	Yes (diacetol)	No	No	Yes	Yes (weak, likely not clinically significant)
Elimination	Renal 40%	Renal 50%	Renal 50%	Renal 16% mainly excreted as metabolites (<2% unchanged) Feces 60%	Renal <1-2%
Half-Life	3-4 hours Active metabolite, diacetol: 12 h	6-9 hours	9-12 hours	6-10 hours	9 minutes Acid metabolite: 3.7 h (likely not clinically significant) Methanol: several days (likely not clinically significant)

BETA-ADRENERGIC RECEPTOR BLOCKING AGENTS

Generic Name	**Acebutolol**	**Atenolol**	**Bisoprolol**	**Carvedilol**	**Esmolol IV**
Dosage Adjustment	Moderate-severe renal dysfunction: 50-75% dose reduction	Moderate- severe renal dysfunction: CrCl 10-30 mL/min reduce dose 50% CrCl <10 mL/min reduce dose to 25%	Moderate-severe renal and hepatic dysfunction: initial dose 2.5 mg	Moderate-severe liver failure: dosage guidelines not available In liver cirrhosis: suggested initiation with 20% of normal dose Contraindicated in clinically manifest hepatic impairment	No adjustment guidelines in renal/hepatic dysfunction. Metabolite excreted unchanged in kidney and plasma level can increase in end-stage renal disease
Common Drug Interactions[a]	• Amiodarone - ↑ effect, e.g., bradycardia • Calcium Channel Blockers – potentiate effects or toxicity of either group of drugs • Clonidine - hypertensive reactions when clonidine withdrawn • Digoxin - ↑ risk of bradycardia especially with non-ISA selective beta blockers • Epinephrine, phenylephrine, adrenergic drugs – hypertensive reactions especially with non-cardioselective beta blockers • Oral hypoglycemics - potential hyperglycemia due to beta blocker inhibition of insulin release and ↓ tissue uptake • Insulin - may affect glucose metabolism • Non-steroidal anti-inflammatory agents - ↓ hypotensive effect of beta blockers • Theophylline - all beta blockers antagonize effects • Alpha blockers – may ↑ first dose hypotensive response to alpha blocker				
Specific Drug Interactions[a]		↓ atenolol level; antacid-magnesium hydroxide/aluminum oxide; separate by at least 2 hours		↑ digoxin level ↑ cyclosporine level Metabolised by 2D6; 2C9 ↑ carvedilol level: cimetidine ↓ carvedilol level: rifampin	↑ digoxin level (by 10-20%) ↑ succinylcholine duration of neuromuscular blockade (from 5 to 8 minutes) ↑ esmolol level: IV morphine (by 46%)

BETA-ADRENERGIC RECEPTOR BLOCKING AGENTS

Generic Name	**Acebutolol**	**Atenolol**	**Bisoprolol**	**Carvedilol**	**Esmolol IV**
Unit Cost[b]	$0.08/100 mg $0.12/200 mg $0.25/400 mg	$0.14/50 mg $0.24/100 mg	$0.10/5 mg $0.15/10 mg	$0.34/3.125 mg $0.34/6.25 mg $0.34/12.5 mg $0.34/25 mg	$114.68 (2500mg/250ml bag) $12.36 (100mg/10ml vial)
30 Day[#] Patient Cost	$5 (100 mg bid) $7.80 (200 mg bid) $8 (400 mg daily)	$4.50 (50 mg daily) $7.80 (100 mg daily)	$3.20 (5 mg daily) $4.90 (10 mg daily)	$11 (bid dosing)	
ODB[*]	Yes	Yes	Yes	Yes	No
MSH[b]	Yes	Yes	Yes	Yes	Yes
UHN[b]	Yes	Yes	Yes	Yes	Yes

* List prices from the Ontario Drug Benefit (ODB) Formulary, Ontario Ministry of Health. Last Updated: 01/04/2011 Version 2.2. All prices represent the generic medication option. IV prices come from distributor database.
# 30 day patient costs represented by ODB generic price + 8% markup. These prices do not include a dispensing fee, which can range from 4.99 – 11.99. Pricing is based on a typical dosing regimen.

a - Clinically important pharmacokinetic drug interactions; not meant to be all-inclusive. Refer to additional references for more detail.
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BETA-ADRENERGIC RECEPTOR BLOCKING AGENTS

Generic Name	**Labetalol**	**Labetalol IV**	**Metoprolol**	**Metoprolol IV**
Trade Name	TRANDATE, generics	LOPRESOR, BETALOC, generics	generics	TRASICOR
Dosage Forms	100 mg, 200 mg tablet	IV	25 mg, 50 mg, 100 mg, tablet 200 mg SR tablet	IV 5 mg/5 mL vial
Cardioselective	0	0	+	+
Partial Agonist/ISA*	0	0	0	0
Lipid Soluble	high	high	moderate	moderate
Dosing (usual)				
initial	100 mg bid	Intermittent infusion: 5-20 mg	25-50 mg bid	Myocardial Infarction: 2-5 mg q5min x 3 doses;
maximum	1200 mg (divided in 2-3 doses)	Continuous infusion: 0.25-1 mg/min titrated to response; max. rate: 3 mg/min Usual daily dose range: 300-1200 mg *(based on UHN guidelines, which may differ from manufacturer's)*	200 mg bid ***Note:*** 100 mg bid = 200 mg SR daily	max. 15 mg; then followed by PO beta-blocker
Dosing in CHF	N/A	N/A		N/A
initial			6.25-12.5 mg daily (consider SR)	
target			100 mg bid	
Bioavailability	25-40% Increased with food	100%	50% 65-70% (SR tab) ↑ by food	100%
Onset	1-2 hours	Peak 5-20 minutes	1 hour	20 min
Peak	2-4 hours		1.5-2 hours 3.3 hours (SR tab)	3.5 hours

BETA-ADRENERGIC RECEPTOR BLOCKING AGENTS

Generic Name	**Labetalol**	**Labetalol IV**	**Metoprolol**	**Metoprolol IV**
*** ISA** = intrinsic sympathomimetic activity				
Metabolism	Liver (extensive)		Liver	
Active Metabolite	No	Yes	No	Yes
Elimination	Renal 5%		Renal 5%	Renal 25% Feces 70%
Half-Life	6-8 hours	5.5 hours	3.5 hours	1-9 hours
Dosage Adjustment	Moderate-severe liver failure: 50% reduction No adjustment needed in renal failure		Severe liver failure: dosage guidelines not available	
Common Drug Interactions[a]	• Amiodarone - ↑ effect, e.g., bradycardia • Calcium Channel Blockers – potentiate effects or toxicity of either group of drugs • Clonidine - hypertensive reactions when clonidine withdrawn • Digoxin - ↑ risk of bradycardia especially with non-ISA selective beta blockers • Epinephrine, phenylephrine, adrenergic drugs – hypertensive reactions especially with non-cardioselective beta blockers • Oral hypoglycemics - potential hyperglycemia due to beta blocker inhibition of insulin release and ↓ tissue uptake • Insulin - may affect glucose metabolism • Non-steroidal anti-inflammatory agents - ↓ hypotensive effect of beta blockers • Theophylline - all beta blockers antagonize effects • Alpha blockers – may ↑ first dose hypotensive response to alpha blocker • Lidocaine - ↓ lidocaine clearance with metoprolol; ↑ lidocaine levels by 20-30%			
Specific Drug Interactions[a]			↓ lidocaine, theophylline clearance Metabolized by CYP 2D6 <u>↑ metoprolol level</u>: bupropion, celecoxib, cimetidine, fluoxetine, hydralazine, hydroxychloroquine, paroxetine, propafenone, ritonavir, terbinafine <u>↓ metoprolol level</u>: phenobarbital, rifampin	

a - Clinically important pharmacokinetic drug interactions; not meant to be all-inclusive. Refer to additional references for more detail.

BETA-ADRENERGIC RECEPTOR BLOCKING AGENTS

Generic Name	Labetalol	Labetalol IV	Metoprolol	Metoprolol IV
Unit Cost*	$0.33/100 mg $0.58/200 mg	$27.80 (100mg/ 20ml) injection	$0.06/50 mg $0.14/100 mg $0.14/100 mg SR $0.26/200 mg SR	$7.21 (5mg/5ml vial)
30 Day # Patient Cost	$21.40 (100 mg bid) $37.60 (200 mg bid)		$3.90 (50 mg bid) $9.10 (100 mg bid) $4.50 (100 mg SR daily) $8.40 (200 mg SR daily)	
ODB*	Yes	Yes	Yes	No
***MSH**[b]*	Yes	Yes	Yes	Yes
***UHN**[b]*	Yes	Yes	Yes	Yes

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# 30 day patient costs represented by ODB generic price + 8% markup. These prices do not include a dispensing fee, which can range from 4.99 – 11.99. Pricing is based on a typical dosing regimen.

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BETA-ADRENERGIC RECEPTOR BLOCKING AGENTS

Generic Name	**Pindolol**	**Propranolol**	**Propranolol IV**	**Sotalol**	**Timolol**
Trade Name	VISKEN, generics	INDERAL LA, generics	generics	generics	generics
Dosage Forms	5 mg, 10 mg, 15 mg tablet	10 mg, 20 mg, 40 mg, 80 mg, 120 mg tablet 60 mg, 80 mg, 120 mg, 160 mg LA tablet	IV 1 mg/mL	80 mg, 160 mg tablet	5 mg, 10 mg, 20 mg tablet [Eye drops (various combinations and strengths)]
Cardioselective	0	0	0	0	0
Partial Agonist/ISA*	+++	0	0	0	0
Lipid Soluble	Moderate	High	High	Low	Low to moderate
Dosing (usual)					
initial	5 mg bid with meals	40 mg/day (bid-tid)	Bolus: 1-3 mg every 5 min x 2 doses	40-80 mg bid	10 mg/day (daily-bid)
maximum	45 mg/day (bid-tid dosing)	480 mg/day (bid-tid)	Infusion: 1 to 6 mg/h	320 mg/day (daily-bid)	60 mg/day (bid-tid)
Dosing in CHF	N/A	N/A	N/A	N/A	N/A
Bioavailability	90%	25-35%	100%	90-100% ↓ by food	50-75%
Onset ***Peak***	Peak 2 hours	Peak 1-2 hours	Peak 2-10 min	Peak 2-3 hours	Peak 0.5-3 hours
Metabolism	Liver 60%	Liver 50-70%		Minor liver metabolism	Liver 80%
Active Metabolite	No	Yes		No	No
Elimination	Renal 40%	Renal <1%	Renal <1%	Renal 75%	Renal 20%
Half-Life	3-4 hours	3.5-6 hours (10 hour LA)	2-3 hours	7-15 hours	2-4 hours

*** ISA** = intrinsic sympathomimetic activity

BETA-ADRENERGIC RECEPTOR BLOCKING AGENTS

Generic Name	**Pindolol**	**Propranolol**	**Propranolol IV**	**Sotalol**	**Timolol**
Dosage Adjustment	Severe liver failure: dosage guidelines not available	Severe liver failure: dosage guidelines not available		Use with caution in renal insufficiency (CrCl <60 mL/min) or consider therapeutic alternatives	Moderate-severe liver failure: dosage guidelines not available
Common Drug Interactions[a]	• Amiodarone - ↑ effect, e.g., bradycardia • Calcium Channel Blockers – potentiate effects or toxicity of either group of drugs • Clonidine - hypertensive reactions when clonidine withdrawn • Digoxin - ↑ risk of bradycardia especially with non-ISA selective beta blockers • Epinephrine, phenylephrine, adrenergic drugs – hypertensive reactions especially with non-cardioselective beta blockers • Oral hypoglycemics - potential hyperglycemia due to beta blocker inhibition of insulin release and ↓ tissue uptake • Insulin - may affect glucose metabolism • Non-steroidal anti-inflammatory agents - ↓ hypotensive effect of beta blockers • Theophylline - all beta blockers antagonize effects • Alpha blockers – may ↑ first dose hypotensive response to alpha blocker • Lidocaine - ↓ lidocaine clearance with propranolol; ↑ lidocaine levels by 20-30%				

BETA-ADRENERGIC RECEPTOR BLOCKING AGENTS

Generic Name	**Pindolol**	**Propranolol**	**Propranolol IV**	**Sotalol**	**Timolol**
Specific Drug Interactions[a]		↓ lidocaine, theophylline clearance ↑ hydrochlorothiazide-induced high triglyceride and blood sugar levels Extensive drug interactions, consult web site of CPS CYP 2D6 metabolism ↑ propranolol level: cimetidine, fluoxetine, fluvoxamine, hydralazine, nifedipine ↓ propranolol level: rifampin; antacid (magnesium hydroxide/ aluminum oxide) - separate by at least 2 hours		May ↑ QT or risk of torsades with tricyclic antidepressant, fluoxetine, foscarnet erythromycin, amiodarone or other QT prolonging drugs Concomitant use with diuretics requires careful monitoring of electrolytes ↓ sotalol level : antacid (magnesium hydroxide/aluminum oxide); separate by at least 2 hours	↑ digoxin level CYP 2D6 metabolism ↑ timolol level: cimetidine, ritonavir, quinidine,
a - Clinically important pharmacokinetic drug interactions; not meant to be all-inclusive. Refer to additional references for more detail.					
Unit Cost*	$0.14/5 mg $0.23/10 mg $0.34/15 mg	$0.07/10 mg $0.11/20 mg $0.12/40 mg $0.20/80 mg $0.31/120 mg	$14.17 (1mg/ml vial)	80 mg (not an ODB benefit) $0.65/160 mg	$0.16/5 mg $0.26/10 mg $0.50/20 mg
30 Day# Patient Cost	$9.10 (5 mg bid) $14.90 (10 mg bid) $22 (15 mg bid)	For 240 mg daily dose $54.40 (10 mg tabs) $42.80 (20 mg tabs) $23.30 (40 mg tabs) $19.40 (80 mg tabs) $20.10 (120 mg tabs)		$21.10 (160 mg daily)	For 20 mg daily dose $20.70 (5 mg tabs) $16.80 (10 mg tabs) $16.20 (20 mg tab)
ODB*	Yes	Yes	No	Yes	Yes
MSH[b]	No	Yes	Yes	Yes	No
UHN[b]	Yes	Yes	Yes	Yes	Yes

BETA-ADRENERGIC RECEPTOR BLOCKING AGENTS

Generic Name	Pindolol	Propranolol	Propranolol IV	Sotalol	Timolol

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The contents of this Handbook are approved and endorsed by the UHN Cardiovascular Subcommittee of the Pharmacy and Therapeutics Committee.

1. **Purpose of the Pharmacotherapy Handbook.**

Notice to Healthcare Providers:

The Pharmacotherapy Handbook is intended to be used as a tool to aid in the appropriate prescribing and administration of cardiovascular formulary agents.

This information in this Handbook is intended for use by and with experienced physicians and pharmacists. The information is not intended to replace sound professional judgment in individual situations, and should be used in conjunction with other reliable sources of information. Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about Cardiovascular illness and the treatments in question.

Due to the rapidly changing nature of cardiovascular treatments and therapies, users are advised to recheck the information contained herein with the original source before applying it to patient care.

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Not Medical Advice. The information contained in the Handbook is not a substitute for professional medical advice, diagnosis or treatment. Never make changes to your medication, nor adjust your dose, without first consulting your health care provider. Always seek the advice of a physician or other qualified healthcare provider concerning questions you have regarding a medical condition, and before starting, stopping or modifying any treatment or medication. Never delay obtaining medical advice or disregard medical advice because of something you have or have not read in the Handbook. If you have, or suspect you have, a health problem, or if you experience an adverse side effect, please consult your doctor. If you have, or suspect you are experiencing a health emergency, please call 911 and/or promptly visit a Hospital Emergency Department in your area.

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