

What is the difference? Within class comparisons of psychotropic agents with new products

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When 'new' psychotropic medications are released on the market, it can be difficult to discern the differences between the newer agents and their similar predecessors. Since head to head clinical trials are rarely available, it is important to learn what can be gleaned from the package

inserts and the Food and Drug Administration (FDA) website. These sources are a wealth of information and were used as the primary resources for the comparative tables that follow.

Table 1. Serotonin Norepinephrine Reuptake Inhibitors-FDA Approvals

Agent	Available strengths	FDA approved indications	MFR/Generic avail	Initial Approval
Venlafaxine HCl immediate release tablets ¹	25 mg, 37.5 mg, 50 mg, 75 mg, 100 mg	MDD	only generic available	1993
Venlafaxine HCl XR capsules ²	37.5 mg, 75 mg, 150 mg	MDD, GAD, SAD, Panic Disorder	Pfizer/Wyeth Yes (2013)	1997
Venlafaxine HCl ER tablets ³	37.5 mg, 75 mg, 150 mg, 225 mg	MDD, SAD	Osmotica Yes	2008
Desvenlafaxine succinate ER tablets ⁴	50 mg & 100 mg	MDD	Wyeth / yes (as base and fumarate salt)	2008
Desvenlafaxine ER tablets ⁵	50 mg & 100 mg	MDD	Osmotica Desvenlafaxine base	2013
Desvenlafaxine ER tablets ⁶	50 mg & 100 mg	MDD	Alembic Desvenlafaxine base	2013
Desvenlafaxine fumarate ER tablets ⁷	50 mg & 100 mg	MDD	Teva	2013
Milnacipran tablets ⁸	12.5 mg, 25 mg, 50 mg, 100 mg	Fibromyalgia	No	2009
Levomilnacipran extended release capsules ⁹	20 mg, 40 mg, 80 mg, 120 mg	MDD	No	2009
Duloxetine delayed release capsules ¹⁰	20 mg, 30 mg, 60 mg	MDD, GAD, fibromyalgia, chronic OA pain, CLBP, DNP	December 2013 ¹¹	2004

MDD = major depressive disorder; GAD = generalized anxiety disorder; SAD = social anxiety disorder; OA = osteoarthritis; CLBP = chronic low back pain; DNP = diabetic nerve pain

Table 2. Serotonin Norepinephrine Reuptake Inhibitors-Pharmacokinetic Comparison

Agent	t _{max} (hours)	C _{max} ng/mL	t _{1/2}	TE Code	Differences/Metabolism/ Comments
Venlafaxine HCl immediate release tablets ¹ (75 mg BID)	2 3 ODV	225 290 ODV	5 ± 2 11±2 ODV	AB*	Solubility =572 mg/mL in water
Venlafaxine HCl XR capsules ² (150 mg dose)	5.5 9 ODV	150 260 ODV	5 ± 2 11±2 ODV	AB*	Once daily administration
Venlafaxine HCl ER tablets ³ (75 mg dose)	6.3 ± 2.3 11.6 ± 2.9 ODV	26.9 ± 13.4 97.9 ± 29.4 ODV	10.7 ± 3.2 12.6 ± 3 ODV	AB*	Not considered interchangeable with XR capsules
Desvenlafaxine succinate ER tablets ¹²	7.5 (not in most recent PI)	Not provided	11 (not in most recent PI)	None	Soluble in water
Desvenlafaxine ER tablets Khadezla ⁵	6 (3-14)	Not provided	9.5 (± 1.5)	BC	Sparingly soluble in dimethyl sulfoxide BC rated
Desvenlafaxine ER tablets ⁶	Not provided	Not provided	Not provided	BC	Sparingly soluble in dimethyl sulfoxide BC rated
Desvenlafaxine fumarate ER tablets ⁷	7.5 (4.5-14)	Not provided	9.8 hours	None	Slightly soluble in water
Milnacipran ⁸	2-4	Not provided	6-8	None	Soluble in water <i>d</i> -milnacipran half-life 8-10 hrs vs <i>l</i> -milnacipran 4-6 hrs 55% renal elimination of parent No significant interactions
Levomilnacipran extended release tablets ⁹	6-8	341	12	None	58% renal elimination CYP 3A4
Duloxetine delayed release capsules ¹⁰	6 (10 with food)	Not provided	12 (8-17)	None	CYP 2D6 inhibitor 2D6, 1A2 substrate

ODV = o-desvenlafaxine; *: AB rated generic products are available; the three venlafaxine products are not AB rated to each other

Table 3. Selective Serotonin Reuptake Inhibitors

	Generic Available	Original FDA release date ¹¹	Difference from parent	Available on discount lists ^{13,14}
Citalopram				
Tablet	Yes	1998	--	Y
Oral solution	Yes	1999	Liquid	N
Escitalopram				
Tablet	Yes	2002	Single isomer	N
Oral solution	Yes	2002	Liquid	N
Fluoxetine				
Capsule	Yes	1987	--	Y
Sarafem®	Yes	2000	Capsule color	N
Prozac weekly™	Yes	2010	Delayed release	N
Oral solution	Only	1991	Liquid	N
Tablet 10, 20, 40 mg	Only	1999	Tablet form	Y
Tablet 60 mg ¹⁵	Only	2011	Tablet strength	N
Fluvoxamine				
Tablet	Only	1994	--	N
Luvox CR®	Yes	2008	Controlled release	N
Paroxetine				
Tablet	Yes	1992	--	Y
Suspension	No	1997	Liquid	N
Paxil CR®	Yes	1999	Controlled release	N
Pexeva®	No	2003	Mesylate salt tablet	N
Brisdelle™	No	2013	Mesylate salt capsule	N
Sertraline				
Zoloft	Yes	1991	--	N
Liquid concentrate	Yes	1999	Liquid	N

Table 4. Bupropion Products¹¹

	Generic Available	Original FDA release date ¹¹	Difference from parent	Available on discount lists ^{13,14}
Bupropion				
Wellbutrin®	Yes	1985	---	N
Wellbutrin SR®/Zyban	Yes	1996	Twice daily	N
Wellbutrin XL®	Yes	2003	Once daily	N
Aplenzin™	Pending 2013	2008	Salt form	N
Forfivo™ XL	No	2011	450 mg tablet	N

Table 5. Guanfacine IR vs Intuniv (note: Pharmacokinetics based on adult data)

	C _{max} (ng/mL)	AUC (ng.h/mL)	Bioavailability	t _{max} (hrs)	t _{1/2} (hrs)	Generic available
Intuniv 1 mg daily (fasted state) ¹⁶	1	32	58% of IR	6	18	No ^{**}
Guanfacine 1 mg once daily (fasted state) ¹⁷	2.5	56	100%	3	16	Yes
Intuniv 1 mg after high fat breakfast ¹⁶	1.75	45	80% of IR	NR	NR	No ^{**}
Kapvay 0.1 mg fasted ¹⁸	258	6729	92% of IR	6.5	12.65	No ^{***}
Clonidine 0.1 mg ¹⁹	443	7313	100%	2.07	12.57	Yes
Kapvay 0.1 mg after high fat meal ¹⁸	235	6505	89%	6.8	12.67	No ^{***}

*Dosing recommendations, cost and dose adjustments for drug interactions in article in this month's issue

**Generic tentatively approved May 2013, however not released as of December 2013¹¹

*** AB rated generic product approved September 30, 2013¹¹

Table 6. Amphetamine Based Products

Brand Name	t _{max} hrs	t _{1/2} hrs	Dosing Interval Comments	Conversion from IR Adderall
Adderall IR ²⁰	3	9	Twice daily	
Adderall XR ²⁰	7	9-11	Once daily Food prolongs t _{max} 2.5 hrs Capsule may be sprinkled	1:1
Dexedrine Spansules ²¹	3	12	Capsule may be sprinkled	NA
Methamphetamine ²²	NA	4	Once or twice daily	NA
Vyvanse ^{23, 24}	5-6		Once daily dosing	70 mg Vyvanse = 30 mg Adderall XR

Table 7. Valproate Products²⁵⁻²⁹

	Valproic acid	Divalproex delayed release	Divalproex Sprinkle capsules	Divalproex extended release tablets	Valproic acid extended release capsules
t _{max} (h)	1-4	4	3-3	4-17	2
t _{max} w/food (h)	NA	8	4.8	NA	4.8
Bioavailability compared to valproic acid	NA	1:1	1:1	8-20% lower	1:1
Dosage forms	250 mg/5 mL 250 mg capsule	125 mg, 250 mg, 500 mg tablet	125 mg capsule	250 mg, 500 mg tablet	125 mg, 250 mg, 500 mg capsules
Recommended dosing interval	'divided doses'	'divided doses'	'divided doses'	Daily	Daily
Original FDA Approval	1978	1983	1989	2002	2008
Generic	Yes	Yes	Yes	Yes	No

Table 8. Atypical Antipsychotics¹¹

	Generic Available	Original or tentative FDA approval date	Difference from parent
Clozapine			
Clozaril®	Yes	1989	--
Fazaclo®	Yes	2004	ODT
Versacloz™	No	2013	Suspension
Risperidone			
Risperdal®	Yes	1993	--
Solution	Yes	1996	Liquid
Risperdal M-Tab®	Yes	2003	ODT
Risperdal Consta®	No	2003	LAI
Paliperidone			
Invega®	No	2006	Metabolite, once daily
Invega Sustenna®	No	2009	LAI
3 month Sustenna®	No	Pending	3 month LAI
Olanzapine			
Zyprexa®	Yes	1996	--
Zyprexa® Zydis®	Yes	2000	ODT
Zyprexa® IM	Yes	2004	Injection
Relprevv™	No	2009	LAI
Quetiapine			
Seroquel®	Yes	1997	--
Seroquel XR®	No	2007	Extended release
Aripiprazole			
Abilify®	No	2002	--
Solution	No	2004	Liquid
Abilify Discmelt®	No	2006	ODT
Abilify® IM	No	2006	Injection
Abilify Maintena™	No	2013	LAI
Ziprasidone			
Geodon®	Yes	2001	--
Geodon® IM	Yes	2002	Injection

ODT = orally disintegrating tablet; LAI = long acting injection; IM = short acting intramuscular injection

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