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Guideline for Evaluation and Treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in Adults

SCOPE: The Guideline for Evaluation and Treatment of Attention-Deficit/ Hyperactivity Disorder (ADHD) in Adults is intended to offer diagnostic and prescribing assistance for providers, clients, and the interested general public to increase the safety and quality of ADHD treatment in adults. It is not intended to be comprehensive in scope. Selection of therapy for individual clients is ultimately based on the health care provider's assessment of clinical circumstances and client needs. The recommendations here are intended to assist practitioners in providing consistent, high quality care. Providers must carefully consider and incorporate the clinical characteristics and circumstances of each individual client.

INTRODUCTION: In the past, psychiatrists believed that children and adolescents outgrew ADHD, but in recent years, it has become clear that about half of this group have a persistent disorder into adulthood. The current prevalence is estimated to be 4.4% in the United States. ADHD in adults can be accompanied by serious impairment, including poor learning and limited educational achievement, poor job performance and job loss, interpersonal and marital problems, an increased rate of arrest for speeding and an increased rate of traffic accidents. Mortality is higher in persons with ADHD than in the general population. Co-existing psychiatric disorders are common, and include mood, anxiety, substance use, intermittent explosive, and antisocial personality disorders.

Rates of ADHD in non-psychotic adult community mental health centers are believed to be 10% or higher, yet few of these clients are identified and treated. This is true despite the fact that stimulants have effect sizes comparable to the use of antidepressants in depression or antipsychotics in psychosis. Treatment has been shown to reduce the risk of criminal convictions, accidental injuries, substance use disorders, and suicide. Occupational and social functioning may also improve with treatment.

Possible reasons for this under-diagnosis and under-treatment are numerous. A significant one, which this guideline hopes to address, is inadequate awareness and training in the diagnosis and management of the disorder. Clinicians should find training or study on their own to remedy these gaps and provide adequate assessment and treatment of this disorder.

Treatment of adult ADHD in the community mental health care (CMHC) setting is complicated by:

- co-existing psychiatric disorders that may mimic or mask the symptoms of ADHD
- difficulty obtaining or corroborating a history of symptoms prior to the age of twelve (required for the diagnosis)
- inaccurate reporting of attention by the client requiring collateral history from friends or family
- medical disorders that could affect the safety of ADHD medication treatment

- the frequent co-occurrence of substance use disorders in the CMHC population, raising the risk of abuse or diversion of stimulant medications and the question of when, if ever, after remission from a substance use disorder, stimulant medications might be considered

ASSESSMENT: All behavioral health services (BHS) clients should be screened for ADHD as part of their assessment process. Attention should be paid to individuals with non-episodic forms of emotional instability and diagnoses like dysthymia, cyclothymia, and personality disorders. ADHD may be suspected at the point of intake by the clinician doing an initial assessment, by the prescriber during a psychiatric assessment, or any time after admission.

Screening consists of a survey of the client's early school performance and later job history, looking for childhood and adult ADHD symptoms, and evidence of impairment of functioning. At times, major psychiatric illness beginning early in life, severe psychosocial disruption, or serious abuse and/or neglect may make it impossible to separate ADHD symptoms from symptoms caused by these factors.

Diagnosis is made with the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria. It requires the presence of symptoms prior to the age of twelve. However, it does not require impairment before the age of twelve nor does it require that the client met criteria for the full disorder in the pre-teen years. Several recent studies show that a sizeable proportion of adults with ADHD did not meet criteria as children. The meaning of this is debated. One possibility is that intelligent, non-disruptive individuals may not show signs of ADHD until they encounter more challenging task demands later in life.

Attempts should be made to gather records or other information pertinent to diagnosing ADHD in adults. These include school records, prior treatment records, and corroborating history from family and friends.

Family history may be helpful but needs to be expanded beyond the presence of known disorders (like ADHD or a learning disability). Poor job performance, unstable relationships, legal difficulties, anger issues, depression or anxiety, or substance use disorders all may be markers of ADHD in a relative.

ASSESSMENT SCALES: Assessment scales may be used as screening tools to trigger further evaluation. Assessment scales are not sufficient to make the diagnosis independent of a clinical interview. Assessment scale items may point to specific areas or activities in the client's life that require further exploration. They may help by pointing to areas or activities in which the client can give examples of the scale item in their own lives.

It may be beneficial to use the same scale at the time of diagnosis and again later to track response to treatment. Useful scales are brief and directly related to DSM-5 ADHD criteria. Examples include the Self-Report Adult Symptoms and Role Impairment Inventory (ASRS) (Figure 1) and the Third Party Adult ADHD Symptoms and Role Impairment Inventory (Figure 2). Any scale used should be signed, dated, and included in the medical record.

CARDIAC AND MEDICAL SCREENING: Research has shown no overall increase in major cardiac events with the use of stimulants to treat ADHD in adults. However, individual clients at higher cardiovascular risk may require a medical or cardiology referral. Cardiac screening involves asking about a possible heart problem or having a history of chest pain, palpitations, or syncope; and taking a family history of sudden death, heart attacks, and high blood pressure.

The average increase in resting heart rate is 5.7 beats per minute and in blood pressure is 1.2 mmHg with stimulant therapy. The Federal Drug Administration (FDA) warns that stimulants and atomoxetine should not be used in clients with serious heart issues or clients in whom increased blood pressure or heart rate would be problematic. Routine electrocardiogram (ECG) is not required. Some medical conditions such as thyroid disease or sleep disorders may present with symptoms that can mimic ADHD. They should be evaluated for and ruled out as part of the assessment process.

CO-MORBID PSYCHIATRIC DISORDERS AND SUBSTANCE USE DISORDERS: In general, co-morbid psychiatric disorders that have a higher impact on functional impairment should be treated first.

Stimulant medications can trigger or worsen psychotic and manic symptoms, hypertension, and tic disorders. A careful substance use history is a recommended part of the evaluation for ADHD in adults. There are no clear guidelines about when, if ever, it may be appropriate to use stimulants in individuals recovering from a substance use disorder.

STIMULANT PHARMACOTHERAPY: Stimulants (methylphenidate and amphetamine) are the most effective medications for the treatment of ADHD. Methylphenidate and amphetamine are equally effective. There are no recommendations to start with one as opposed to the other. Effects are generally seen within one hour with both immediate-release and controlled-release formulations. The effective dose varies widely between individual agents (Appendix 1 and 2). Some insurance plans prefer one formulation over another.

General principles of stimulant treatment for ADHD in adults include:

- Start with long-acting formulations
- Avoid use of short-acting preparations due to increased potential for abuse
- Start with lower doses and increase according to symptom relief, functional improvement and tolerance
- Use long-acting medications as a base and, if necessary, fill in with short-acting agents to cover periods of waning benefit from the long-acting agent
- Use medications every day, or only when a specific need is identified such as work demands or other tasks
- Take periodic medication holidays to reassess the need for ongoing stimulant treatment

Adverse effects are similar among methylphenidate and amphetamine formulations. Common adverse effects include headache, dry mouth, decreased appetite, weight loss, insomnia, dysphoria and anxiety. Adverse effects of one stimulant formulation may call for trials of other formulations of the same agent or a different medication.

Monitoring should include blood pressure, heart rate, and weight at initial evaluation, at every visit early in treatment, and at a minimum every three months thereafter.

The California prescription drug monitoring system, CURES, should be searched for each client for whom stimulant medication may be used. New guidelines suggest urine toxicology screens, a controlled substance agreement, and careful monitoring of medications prescribed and filled for all individuals receiving stimulant medications. Providers should consider using a controlled substance agreement or medication contract (Figure 3).

Concern about substance use should be discussed with clients. Within San Francisco, referral to the Treatment Access Program (TAP) 415-255-3629 should be made when appropriate.

There is a risk of medication diversion with stimulant prescriptions. This should be regularly monitored for and, if present, should be thoroughly discussed with clients. Once identified, clinicians should take appropriate steps to prevent future diversion, including withholding stimulant medication prescriptions, offering non-stimulant pharmacotherapy and other interventions.

NON-STIMULANT PHARMACOTHERAPY: Non-stimulant medications may be used when stimulant medications are contraindicated. Non-stimulant medications include atomoxetine, alpha 2-agonists (clonidine and guanfacine), and bupropion. The only FDA-approved non-stimulant medication for ADHD in adults is atomoxetine. There is no evidence that atomoxetine has a better safety profile than stimulant medications. It should be used cautiously in clients with cardiovascular disease (including hypertension) or cerebrovascular disease (Appendix 2). Some insurance plans prefer one type of non-stimulant medication over others.

SPECIAL POPULATIONS:

Pregnancy: All medications for the treatment of ADHD in adults are pregnancy category C with the exception of guanfacine, which is category B.

Lactation:

Stimulants: Methylphenidate is excreted in breast milk, resulting in relative infant doses of 0.16% to 0.7% of the weight adjusted maternal dose. Dextroamphetamine, lisdexamfetamine, and mixed amphetamine salts are excreted in breast milk and use may decrease milk production. The manufacturers of methylphenidate, desmethylphenidate, and dextroamphetamine do not give any specific recommendations for nursing. The manufacturer of lisdexamfetamine and mixed amphetamine salts recommends refraining from nursing due to the potential for adverse reactions in a nursing infant.

Non-Stimulants: Clonidine is excreted in breast milk. The manufacturer recommends caution be used if administered to nursing women. It is not known if atomoxetine and guanfacine are excreted in breast milk. The manufacturers of atomoxetine and guanfacine recommend that caution be exercised when administering these medications to nursing women. Bupropion and its metabolites are excreted in breast milk. Recommendations for use in nursing women vary by manufacturer labeling.

Older Adults: This client population has been generally excluded from clinical studies and should be treated with special caution.

Hepatic/Renal Dysfunction: There are special dosing recommendations for hepatic or renal impairment. See Appendix 1, 2 and 3 for which medications require adjustments and refer to package insert for dosing recommendations.

FOLLOW-UP CARE: Follow-up care focuses on functional improvement, not just subjective symptom relief. This may mean contacting family or other informants. Monitoring for adverse effects will usually include tracking weight, blood pressure, heart rate, and sleep.

Early visits are more frequent and involve regular checks of the CURES database. Later visits can be less frequent. The optimal duration of treatment is unknown. The few long-term studies that exist (of 6 to 24 months in duration) suggest that medication benefits are sustained over time. ADHD is considered a chronic condition, but periodic trials off medication may help determine if the medication is still needed.

MAINTENANCE: If treatment was initiated in a mental health setting, stable clients may be considered for transfer to their primary care providers.

Figure 1: Self-Report Adult Symptoms and Role Impairment Inventory

Name: _____ Date: _____
 Time period considered: _____ Medication and dose (if applies): _____

Instructions: This inventory can be used to measure ADHD symptoms. Think of a “typical,” recent week, and complete the lines above. For each item there are questions about effort and consequences. Note on the right how often either of these occur. Use space at the bottom of each page to describe examples of how these symptoms keep you from functioning well in major life roles. If using this form for diagnosis, write down the earliest age each active symptom began to persist.

Inattentive Traits	Rarely	Sometimes	Often	Very Often	Age started
Difficulty being accurate with details					
How often does it take effort to avoid errors? Or: How often do you make “careless” mistakes?	0	1	2	3	
Difficulty sustaining attention					
How often does it take effort to pay attention when in meetings, classes or while reading? Or: How often does your mind wander in meetings, class, or while reading?	0	1	2	3	
Difficulty listening in conversation					
How often is it hard to listen in conversation? Or: How often do you miss what people say to you?	0	1	2	3	
Difficulty sticking to and finishing actions					
How often does it take effort to stick with a task? Or: How often do you leave things unfinished?	0	1	2	3	
Difficulty organizing					
How often is it hard to get around to tasks? Or: How often is there a problem because of poor organization?	0	1	2	3	
Putting off tasks requiring mental effort					
How often is it hard to get around to tasks? Or: How often do you miss a deadline?	0	1	2	3	
Often losing important items					
How often do you take care not to misplace things? Or: How often are you looking for things you misplaced?	0	1	2	3	
Forgetfulness					
How often do you <u>depend on</u> lists or reminders? Or: How often are you upset that you forgot something?	0	1	2	3	
Often distracted by things in environment					
How often do you avoid or tune out distractions? Or: How often are you distracted from tasks?	0	1	2	3	
Total inattentive symptoms score:					_____

Note here examples of how these, or similar difficulties, impact your life roles:
Your own daily activities:
Work or School activities:
Relationship with others:

Hyperactive/ Impulsive Traits	Rarely	Sometimes	Often	Very Often	Age started
Fidgeting How often does it take effort to be still? Or: How often is your fidgeting upsetting to you or others?	0	1	2	3	
Restless How often do you stop yourself from standing Up to the middle of an activity? Or: How often do you get up in middle of activity?	0	1	2	3	
Excessively in motion How often do you stop yourself from walking or running too much? Or: How often are you walking or running when others are not?	0	1	2	3	
Excessively loud How often do you keep yourself from being too loud? Or: How often do you wish you had kept yourself from being too loud?	0	1	2	3	
Excessive internal drive How often do you stop yourself from moving on to another activity? Or: How often is it hard to stick with or enjoy quiet activities?	0	1	2	3	
Talking excessively How often do you stop yourself from talking too much? Or: How often do you wish you had stopped talking sooner?	0	1	2	3	
Speaking at the wrong time in a conversation How often do you stop yourself from interrupting in a conversation? Or: How often do you wish you had waited to speak in turn?	0	1	2	3	
Difficulty waiting How often do you struggle to wait in a line? Or: How often to you avoid lines or leave them?	0	1	2	3	
Intruding on others How often is it hard to stop yourself from interrupting others when they are busy? Or: How often do you intrude on other people?	0	1	2	3	

Total impulsive/ hyperactive Score: _____

Note here examples of how these, or similar difficulties, impact your life roles:

Your own daily activities:

Work or school activities:

Relationships with others:

Developed by Craig B.H. Surman, M.D.

Figure 2: Third Party Adult ADHD Symptoms and Role Impairment Inventory

Name: _____

Date: _____

Time period considered: _____

Medication and dose (if applies): _____

Instructions: This inventory can be completed by a third party (e.g. significant other, family, friend) to help track ADHD symptoms. Ask them to think of a “typical,” recent week. For each item note on the right how often either of these occur, and the earliest age they began persist. Note impact on major life roles at bottom.

Inattentive Traits	Rarely	Sometimes	Often	Very Often	Age Started
Difficulty being accurate with details					
How often do they make “careless” mistakes?	0	1	2	3	
Difficulty sustaining attention					
How often their mind in meetings, class, or while reading?	0	1	2	3	
Difficulty listening in conversation					
How often do they miss what people say to them?					
Difficulty sticking to and finishing actions					
How often do they leave a task before it is unfinished?	0	1	2	3	
Difficulty organizing					
How often is it hard to get around to tasks? Or:		0	1	2	3
How often is there a problem because of poor organization?					
Putting off tasks requiring mental effort					
How often is it hard to get around to tasks? Or:	0	1	2	3	
How often do you miss a deadline?					
Often losing important items					
How often do you take care not to misplace things? Or:	0	1	2	3	
How often are you looking for things you misplaced?					
Forgetfulness					
How often do you depend on lists or reminders? Or:	0	1	2	3	
How often are you upset that you forgot something?					
Often distracted by things in environment					
How often do you avoid or tune out distractions? Or:	0	1	2	3	
How often are you distracted from tasks?					
Total inattentive symptoms score: _____					
Do these symptoms impair function in daily activities, at work or school, or relationships with others? Please note some examples here:					

Hyperactive/ Impulsive Traits	Rarely	Sometimes	Often	Very Often	Age started
Fidgeting					
How often does it take effort to be still? Or:	0	1	2	3	
How often is your fidgeting upsetting to you or others?					
Restless					
How often do you stop yourself from standing up to the middle of an activity? Or:	0	1	2	3	
How often do you get up in middle of activity?					

Excessively in motion

How often do you stop yourself from walking or running too much? Or: How often are you walking or running when others are not? 0 1 2 3

Excessively loud

How often do you keep yourself from being too loud? Or: How often do you wish you had kept yourself from being too loud? 0 1 2 3

Excessive internal drive

How often do you stop yourself from moving on to another activity? Or: How often is it hard to stick with or enjoy quiet activities? 0 1 2 3

Talking excessively

How often do you stop yourself from talking too much? Or: How often do you wish you had stopped talking sooner? 0 1 2 3

Speaking at the wrong time in a conversation

How often do you stop yourself from interrupting in a conversation? Or: How often do you wish you had waited to speak in turn? 0 1 2 3

Difficulty waiting

How often do you struggle to wait in a line? Or: How often do you avoid lines or leave them? 0 1 2 3

Intruding on others

How often do they intrude on other people who are busy? 0 1 2 3

Total Impulsive/ Hyperactive Presentation Score: _____

Developed by Craig B.H. Surman, M.D.

Figure 3: Controlled Medication Agreement (SAMPLE)

Controlled Medication Agreement

Date _____

Name: _____ DOB: _____ BIS: _____

The purpose of this agreement is to prevent misunderstanding about controlled medicines that you will be taking. This agreement will help both you and your Provider to comply with laws regarding controlled pharmaceuticals. This contract also verifies your agreement to participate in non-medication activities that may reduce your symptoms and improve your quality of life.

I, _____ and _____ have decided together to use controlled substance for management of my symptoms. I agree to following contract conditions:

- I agree that this medication will only be used by me and used only as prescribed.
- I will not share, sell or trade my medication with anyone.
- I will safeguard my medication from loss or theft. **Lost, damaged or stolen medicine will not be replaced.**

- If I run out of the medication because I increase the dose without the approval of my prescribing Provider, other clinic Providers will not refill the prescription early.
- I will not seek controlled substance from other Medical Providers outside of this clinic.
- I understand that there may be no refills of my medications without a Provider visit.

- I agree to share my complete medications history in order to avoid adverse drug interactions.

- I will follow through on referral appointments made with other Providers who can help me with my symptoms.

- I agree that upon request, I will bring all unused controlled medication to every office visit.

- I understand that pharmacy records may be reviewed to confirm prescriptions.

- I agree to leave a urine specimen for drug testing upon request, and I understand that failure to do so will be considered a breach of this contract.

- I understand that I must keep my schedule appointments for medication refills, and that I may not come to drop-in appointments for medication refills if I miss a scheduled appointment,

I agree to participate in the following non-medication activities:

I understand that if I break this agreement, my Provider may stop prescribing these medicines.

MEDICATION	INSTRUCTIONS	AMOUNT PER WEEK/MONTH

My Provider has explained that the above medications have possible side effects and may be addictive.

Client Signature: _____

Date _____

Provider Signature _____

Date _____

Appendix 1: Stimulant Medications (Methylphenidate)

Action	Short		Intermediate	Long						
Brand	Focalin	Ritalin, Methylin	Ritalin SR, Metadate ER	Focalin XR	Ritalin LA	Metadate CD	Aptensio XR	Concerta	Quillivant XR	Daytrana
Drug	Dexmethylphenidate	Methylphenidate		Dexmethylphenidate	Methylphenidate					
Generic	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No
Dosing Sizes	2.5, 5, 10 mg tab	5, 10, 20 mg tab; 5mg/5mL, 10 mg/5 mL	Ritalin SR: 20 mg tab Metadate ER: 10, 20 mg tab	5, 10, 15, 20, 25, 30, 35, 40 mg cap	10, 20, 30, 40 mg cap	10, 20, 30, 40, 50, 60, mg cap	10, 15, 20, 30, 40, 50, 60 mg cap	18, 27, 36, 54 mg tab	25mg/5mL (60, 120, 150, 180 mL)	10, 15, 20, 30 mg patch
Max Dose	20 mg/day	60 mg/day	60mg/day	40 mg/day	60 mg/day	60 mg/day	60 mg/day	72mg/day	60 mg/day	30 mg/day
Dosing	BID	BID-TID	Daily	Daily						
Release	IR	IR	ER/SR	Capsule is 50% IR & 50% DR beads.	Capsule is 50% IR & 50% DR beads.	Capsule is 30% IR % 70% DR beads.	Capsule contains multi-layered beads that is 40% IR and 60% CR	Non-absorbable tablet is 22% IR & 78% CR	Suspension is 20% IR and 80% DR	Transdermal
Onset	30	30-60	30-60	30	30-60	30-60	-	60-120	45	120
Duration of Action (hr)	3-5	3-6	8	12	8	8	-	10-12	12	9
Crush?	Yes	Yes	No, Swallow whole with water or other fluid	No, Swallow whole or may be opened and contents sprinkled over a spoonful of applesauce			No, Swallow whole with water or other fluid	-	-	
CYP Enzyme Metabolism	-									
Hepatic/ Renal impairment	No studies available, likely not of concern									
Comments	Take 30-45 min before meal when possible	High fat meal may delay peak by 1.5 hrs	Take 30-45 min before meal when possible	Mimics BID dosing	Mimics BID dosing. High fat meal may delay peak	High fat meal may delay early peak by 1 hr	-	-	Shake vigorously for ≥ 10 sec before administering	Apply to hip. Remove after 9 hrs; absorption may continue for several hours after removal

Appendix 2: Stimulant Medications (Amphetamine)

Action	Short			Intermediate	Long			
Brand	DextroStat, Dexedrine	Evekeo	Adderall	Dexedrine Spansules	Adderall XR	Vyvanse	Dyanavel XR	Adzenys XR-ODT
Drug	Dextroamphetamine	Amphetamine	Mixed Amphetamine Salts	Dextroamphetamine	Mixed Amphetamine Salts	Lisdexamphetamine	Racemic Amphetamine Sulfate	Racemic Amphetamine Sulfate
Generic	Yes	No	Yes	Yes	Yes	No	No	No
Dosing Sizes	5, 10 mg tabs	5, 10 mg tab	5, 7.5, 10, 12.5, 15, 20, 30 mg tabs	5, 10, 15 mg bead-filled caps	5, 10, 15, 20, 25, 30 mg caps	10, 20, 30, 40, 50, 60, 70 mg caps	2.5 mg/mL susp	3.1, 6.3, 9.4, 12.5, 15.7, 18.8 mg ODT
Max Dose	40 mg/day	40 mg/day	40 mg/day	40 mg/day	30 mg/day	70 mg/day	20 mg/day	18.8 mg/day
Dosing	Daily-BID	Daily	BID	Daily	Daily	Daily	Daily	Daily
Release Formulation	IR	Contains d-amphetamine & l-amphetamine salts in a 1:1 ratio	Contains d-amphetamine & l-amphetamine salts in a 3:1 ratio	Capsule is 50% IR and 50% DR beads	Contains d-amphetamine & l-amphetamine salts in a 3:1 ratio. Capsule is 50% IR and 50% DR beads.	IR	Contains d-amphetamine & l-amphetamine salts in a 1:1 ratio	Contains d-amphetamine & l-amphetamine salts in a 3:1 ratio
Onset	30-60	-	30-60	30-60	30-60	-	-	-
Duration of Action	2-6 hrs	-	5 hrs	6-9 hrs	9 hrs	10 hrs	-	-
Crush?	Yes	Yes	Yes	No, Do not chew beads in capsule	No, Sprinkle on applesauce, swallow without chewing	No, Swallow whole or may be opened and entire contents dissolved in a glass of water	-	No, Do not chew or crush tablet
CYP Enzyme Metabolism	2D6							
Hepatic/Renal Impairment	May inhibit metabolism/elimination resulting in prolonged exposure	No information available	May inhibit metabolism/elimination resulting in prolonged exposure				No information available	No information available
Comments	-	-	-	-	Mimics BID dosing	Continuous-release capsule. High fat meal may delay peak by 1 hr	-	Do not push tablet through foil

Appendix 3: Non-Stimulant Medications

Brand	Strattera	Wellbutrin	Wellbutrin SR	Wellbutrin XL	Catapres	Catapres-TTS	Tenex	Intuniv
Drug	Atomoxetine	Bupropion			Clonidine		Guanfacine	
Generic available	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Dosing Sizes	10, 18, 25, 40, 60, 80, 100 mg caps	75, 100 mg tab	100, 150, 200 mg tab	150, 300 mg tab	0.1, 0.2, 0.3 mg tab	0.1, 0.2, 0.3 mg patches	1,2, mg tab	1,2,3,4 mg tab
Max Dose	100 mg/day or 1.4 mg/kg/day	450mg/day	400mg/day	450mg/day	2.4mg/day	0.6mg/day every 7 days	4mg/day	4mg/day
Dosing	QD-BID	TID	BID	Daily	Daily-QID	Once every 7 days	Daily	Daily
Release formulation	N/A	IR	SR	ER	IR	Transdermal Patch	IR	ER
Duration of Action (hr)	24	8	12	24	8	Up to 8 hrs after patch removal	8-14 hrs, up to 24 hrs in higher doses	
Crush?	No	Yes	No	No	Yes	N/A	Yes	No
CYP Enzyme Metabolism	2D6	1A2, 2A6, 2B6, C29, 2D6, 2E1, 3A4			-		3A4	
Hepatic/Renal Impairment	Hepatic	Renal Hepatic			Renal		None	
Comments	High fat meals may delay peak by 3 hrs	-			Do not stop abruptly		Avoid administration with high fat meals. Do not stop abruptly	

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