# DSH PSYCHOTROPIC MEDICATION Operational Procedures

## ALPHA-2 ADRENERGIC AGONISTS PROTOCOL

I. Indications:

A. At least 1 of the following clinical indications is present and documented in the chart prior to treatment. Note that some indications are limited to specific alpha-2 adrenergic agonists:

1. Hypertension (HTN)
2. Attention deficit hyperactivity disorder (ADHD)
3. Oppositional defiant disorder (ODD)
4. Pervasive developmental disorders
5. Motor tics
6. Tourette's syndrome
7. Opioid** and alcohol withdrawal
8. Posttraumatic stress disorder (PTSD) (clonidine)
9. Clozapine-induced hypersalivation (clonidine)
10. Menopausal flushing (clonidine)
11. Severe pain in cancer patients not adequately relieved by opioid analgesics alone (combination with opiates) (clonidine)
12. Migraine headache prophylaxis (guanfacine)
13. Mild-moderate agitation, schizophrenia- associated (dexmedetomidine SL)*
14. Mild-moderate agitation, bipolar-associated (dexmedetomidine SL)*
15. Recurring or persistent agitation, aggressive, self-injurious, stereotypic, or impulsive behaviors with evidence that a behavioral treatment, as part of a formal treatment program, was adequately implemented and found to be ineffective

*Dexmedetomidine is limited to prn use for agitation

**Lofexidine is typically limited to opiate withdrawal

II. Contraindications:

A. Hypersensitivity to guanfacine, dexmedetomidine, lofexidine or clonidine or any component of their formulations

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III. Precautions (risk/benefit analysis supports use):

A. Severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease

B. Hypotension/bradycardia, heart block or syncope

C. Bradycardia

D. Concomitant use of sympatholytic medications or sedating medications

IV. The following initial workup and follow-up evaluations should be completed:

A. There is informed consent or alternate legal authorization

B. Initial work up includes heartrate and blood pressure. ECG if known coronary artery disease

C. Monitoring

1. Observation for excessive sedation following initiation or dose increase

2. At least weekly monitoring of pulse and blood pressure during titration or for at least one week after subsequent dose increases for guanfacine or clonidine

3. Annual ECG

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V. Dose initiation, titration, and discontinuation:

Table 1. Alpha-2 agonist starting doses, titration rate, and maintenance doses.

| MEDICATION | DOSE FORMS | INDICATION | MAXIMUM FOR INDICATION | USUAL STARTING DOSE FOR INDICATION AND TITRATION RATE |
|---|---|---|---|---|
| Guanfacine<br><br><br><br>Guanfacine ER | 1 mg<br>2 mg<br>3 mg<br><br><br>ER tab<br>1 mg<br>2 mg<br>3 mg<br>4 mg | HTN | 3 mg | • IR 1 mg qhs, then increase by 1 mg after 3-4 weeks |
| | | ADHD | 7 mg | • IR 1 mg daily, then increase to 1 mg BID after one week and by 1 mg/week<br><br>• ER 1 mg qd, then increase by 1 mg/week |
| | | Agitation & Impulsivity | 7 mg | • IR 1 mg daily, then increase to 1 mg BID after one week and by 1 mg/week<br><br>• ER 1 mg qd, then increase by 1 mg/week |
| | | Opioid withdrawal | | • 3- 4 mg PO TID |
| | | Migraine prophylaxis | | • 1 mg daily |
| | | Tourette's syndrome | 4 mg/day divided BID- TID | • 0.5 mg BID |
| Clonidine IR<br><br><br><br>Clonidine ER (Kapvay) | Clonidine IR<br>0.1 mg<br>0.2 mg<br>0.3 mg<br><br><br>Clonidine ER (Kapvay) 0.1 mg | HTN | IR 2.4 mg/day, divided<br><br>ER 0.52 mg/day<br><br>Clonidine transdermal 0.6mg/24h qwk | • IR 0.1 mg BID, then increase by 0.1 mg/day each week<br><br>• ER 0.17 mg qhs, then titrate by 0.09 mg/day qwk<br><br>• Transdermal patch 0.1 mg/24h qwk |
| | | ADHD | IR 0.4 mg/day divided doses | • IR 0.05 mg qhs, then increase by 0.05 mg/day each week |

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|---|---|---|---|---|
| Clonidine ER (Nexiclon)<br><br>Clonidine transdermal patch | Clonidine ER (Nexiclon XR)<br>0.17 mg<br>0.26 mg<br><br>Clonidine transdermal<br>0.1 mg/24h<br>0.2 mg/24h<br>0.3 mg/24 h | | ER 0.4 mg/day | • ER 0.1 mg qday- bid, divide doses bid if >0.2 mg/day |
| | | Agitation & Impulsivity | IR 0.4 mg/day divided doses<br><br>ER 0.4 mg/day divided doses | • IR 0.05 mg qhs, then increase by 0.05 mg/day each week<br><br>• ER 0.1 mg qday- bid, divide doses bid if >0.2 mg/day |
| | | Opioid withdrawal | 2.0 mg/day divided | • 0.1 mg TID |
| | | PTSD | IR 0.3 mg/day divided | • IR 0.1 mg qHS |
| | | Tics<br><br>Tourette's Syndrome | IR 0.4 mg divided<br><br>ER 0.4 mg divided<br><br>Transdermal 0.6mg/24h qwk | • IR 0.025-.05 mg<br>• bid-tid<br><br>• ER 0.1 mg qday- bid<br><br>• clonidine transdermal 0.1mg qwk, then increase dose q1-2 wk |
| | | Sialorrhea | IR 0.2 mg/day divided<br><br>ER 0.4 mg/day divided<br><br>Transdermal 0.2 mg/24h qwk | • IR 0.1 mg QHS, then titrate up to 0.1 mg BID, then increase by 0.1 mg/week<br><br>ER 0.4 mg/day divided<br><br>• Transdermal 0.1 mg/24h qwk |
| | | Menopausal flushing | Transdermal 0.3 mg/24h/week | • Transdermal 0.1 mg/24h/week |
| Dexmedetomidine SL | 120 mcg SL film<br><br>180 mcg SL film | Mild-moderate agitation<br><br>Severe agitation | Mild-moderate 240 mcg total daily dose<br><br>Severe 360 mcg total daily dose | • 120 mcg mild-moderate and patients >65 y/o, 2nd or 3rd dose 60 mcg, at least 2 hours apart<br><br>• 180 mcg severe, 2nd or 3rd dose 90 mcg, at least 2 hours apart |

| | | | | |
|---|---|---|---|---|
| Lofexidine | 0.18 mg tablets | Opioid withdrawal | 2.88 mg/day with no single dose >0.72 mg | • 0.18 mg QID, 5-6 hours between doses |

A. With all the alpha 2 adrenergic medications, doses should be held if SBP <90 mmHg, DBP <60 mmHg, HR <60 beats/min, or postural decrease in SBP ≥ 20 mmHg or DBP ≥ 10 mmHg.

B. Guanfacine IR and guanfacine ER have different pharmacokinetic characteristics with guanfacine ER $C_{max}$ approximately 60% of guanfacine IR. Guanfacine ER should not be given with high fat meals as it increases mean exposure of guanfacine ER compared to fasted state.

C. Clonidine IR and clonidine ER have different pharmacokinetic characteristics with clonidine ER $C_{max}$ approximately 50% lower compared to clonidine IR.

D. When switching from clonidine to clonidine transdermal patch, oral dose should be continued for 2 days after initial application.

E. For opiate withdrawal, treatment is continued for the duration the patient experiences withdrawal symptoms (usually between 5-10 days), then tapered off slowly to avoid rebound hypertension.

F. Alpha 2 adrenergic agonists should be tapered off after prolong use except for dexmedetomidine SL

G. Dexmedetomidine SL administration can be sublingual (under tongue), patient should not eat or drink for 15 minutes or buccal (behind lower lip), patient should not eat one hour after buccal administration.

VI. Possible adverse reactions:

A. Sedation (somnolence)

B. Dizziness

C. Fatigue

D. Irritability

E. Weakness (asthenia)

F. Dry mouth

G. Constipation

H. Hypotension

I. Headache

J. Impotence

K. For clonidine transdermal dermatological adverse reactions include erythema, pruritus, allergic contact sensitization, contact dermatitis, and other skin reactions

L. Rare adverse effects

1. Skin rash with exfoliation, syncope, bradycardia, palpitations, substernal pain, abdominal pain, diarrhea, dyspepsia, dysphagia, nausea, amnesia, confusion, depression, insomnia, libido decrease, rhinitis, taste perversion, tinnitus, conjunctivitis, iritis, vision disturbance, leg cramps, hypokinesia, dyspnea, dermatitis, pruritus, purpura, sweating, testicular disorder, urinary incontinence, malaise, paresthesia, paresis, and hallucinations

M. Rare serious effects

1. Acute renal failure, cardiac fibrillation, cerebrovascular accident, congestive heart failure, heart block, and myocardial infarction

VII. Dose is adjusted for special populations:

A. Dexmedetomidine SL requires dose adjustments in patients with hepatic impairment

B. Lofexidine requires dose adjustments in patients with hepatic and renal impairment

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