

Agents for Medication Induced Movement Disorders

A. FDA Approved Indications in Psychiatry:

1. Extrapyramidal Symptoms: (Benztropine, Amantadine, Trihexyphenidyl, Diphenhydramine)
2. Dystonic Reactions, Acute: Bzotropine IM/IV
3. Parkinsonism (Neuroleptic Induced Parkinsonism): Amantadine
4. Insomnia short-term treatment: Diphenhydramine
5. Sedation: Diphenhydramine

B. Non-FDA approved indications commonly used in Psychiatry:

1. Parkinsonism: Bzotropine, Trihexyphenidyl, Diphenhydrmine
2. Akathisia: Propranolol (FDA approved for Essential Tremor), Benzodiazepines

Documentation
Required

C. Minimal documentation

1. All standard outpatient & inpatient requirements
2. Document risk versus benefit in context of the following:
 - A. To prevent EPS; antipsychotics should be used judiciously, at minimum effective dose and for the shortest possible duration.
 - B. When EPS presents:
 1. Reduce the dose if clinically indicated.
 2. Switch to another agent with lower liability to cause EPS.
 3. If 1 & 2 above fails or clinically inappropriate then management with anticholinergics may be initiated at the lowest effective dose for a short duration i.e. three months. It is recommended to taper to discontinuation after the management of acute EPS. This is intended to minimize, polypharmacy, risk of side effects including cognitive impairment and the risk of abuse.
 4. Anticholinergics worsen Tardive Dyskinesia; therefore, they should be avoided and discontinued if TD develops.
 5. Prophylactic use is ONLY recommended for patients at high risk for developing EPS i.e. first psychotic episode in young severely ill. When used prophylactically, anticholinergics may be used at the lowest effective dose, short duration and documentation of the response to above **strategies**

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i.e. consideration of agents with lower liability to cause EPS.

Documentation
Required

D. Maximum dosage – see Medication Summary for MDD

E. Duration

1. For Outpatient: Document rationale when making any medication change.
2. For Inpatient: Document rationale when making more than 3 changes in any 7-day period.

F. PolyPharmacy

Concurrent use of two anticholinergic/antihistaminic agents is considered to be polypharmacy. When considering addition of more than one agent within a class, it is recommended to first titrate the initial agent to maximum tolerated dose; then provide clear supportive rationale for the additional agent(s).

G. Drug-Drug Interactions – Refer to www.epocrates.com

H. Warning & Precautions

1. Glaucoma, angle-closure
2. BPH
3. Caution in elderly patients
4. Caution if cardiovascular disease
5. Caution in renal & hepatic disease
6. Caution if high environmental temperature
7. Caution if GI/GU obstruction
8. Caution with alcohol use

I. Standard laboratory and examination requirements

1. For inpatient: Basic laboratory studies on admission
2. For outpatient: When managing EPS, routine monitoring using an appropriate scale is required. Depending on the symptoms presented; AIMS, BARS or Simson-Angus Scale (SAS) may be used. When anticholinergics are used, monitoring is required at minimum at baseline and annually.

When using anticholinergics prophylactically and patient develops EPS; dosage reduction of neuroleptic or switching to a different neuroleptic with lower liability to cause EPS need to be considered while continuing with the anticholinergic agent, increasing its dose or switching to a

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different anticholinergic agent. In such cases a follow up monitoring by completing one of the above scales is required within three months from the time EPS were detected.

3. Additional monitoring should be considered depending on the clinical situation and whenever there is a change in the patient's status.

J. Pregnancy and Lactation (Table 2)

Attachment 1: Table: Maximum Daily Dose

Attachment 2: Table: Pregnancy and Lactation

Abnormal Involuntary Movement Scale (AIMS)

Barnes Akathesia Rating Scale (BARS)

Simpson-Angus Scale (SAS)

References:

1. Epocrates & Micromedex
2. WHO 1990 statement: Role of anticholinergic medications in patients requiring long-term antipsychotic treatment for psychotic disorders
3. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2306233/pdf/canfamphys00259-0169.pdf>
4. <http://www.ingentaconnect.com/content/ben/cpd/2004/00000010/00000018/art00013>
5. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3325428/>
6. <http://www.uptodate.com/contents/tardive-dyskinesia-prevention-and-treatment>
7. Tamra Jean Courey, MSN; Detection, Prevention, and Management of Extrapiramidal Symptoms. Journal for Nurse Practitioners. 2007;3(7):464-469
8. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3018852/> Movement disorders induced by antipsychotic drugs: Implication of the CATIE Schizophrenia Trial
9. <http://www.ncbi.nlm.nih.gov/pubmed/24102938> ; Benefits and limits of anticholinergic use in schizophrenia: Focusing on its effect on cognitive function.
10. Julia Eve Desmarais, et al, Anticholinergics in the era of atypical antipsychotics: short-term or long-term treatment?, Journal of psychopharmacology, 26(9) 1167-1174, 2012.

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Table 1: Maximum Daily Dose

Agents	Brand	Max Daily Dose
Amantadine	Symmetrel	300 mg
Benztropine	Cogentin	8 mg
Biperiden	Akineton	16 mg
Trihexyphenidyl	Artane	15 mg

References: Epocrates, Micromedex

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Table 2: Pregnancy Categories & Nursing Mother

Agents	Brand	Pregnancy Category	Nursing Mother
Amantadine	Symmetrel	C	Lactation: Safety Unknown Inadequate literature available to assess risk, Caution advised.
Benztropine	Cogentin	C	Lactation: Safety Unknown Inadequate literature available to assess risk, Caution advised.
Biperiden	Akineton	C	Infant risk cannot be ruled out. Available evidence and/or expert consensus is nonconclusive or is inadequate for determining infant risk when used during breastfeeding. Weigh
Trihexyphenidyl	Artane	C	Lactation: Safety Unknown Inadequate literature available to assess risk, Caution advised.
Diphenhydramine*	Benadryl	B	Lactation: Probably safe Limited information in animals and/or humans demonstrates no risk/minimal risk of adverse effects to infant/breast milk production, Caution advised.
Propranolol*	Inderal	C	Lactation: Probably safe Limited information in animals and/or humans demonstrates no risk/minimal risk of adverse effects to infant/breast milk production, Caution advised.

* Off Label

AIMS Examination Procedure

Instructions:

- Should be completed before entering the ratings on the AIMS form.
 - Either before or after completing the Examination Procedure, observe the patient unobtrusively at rest (i.e., in waiting room).
 - The chair to be used in this examination should be a hard, firm one without arms
-

1. Ask patient whether there is anything in his/her mouth (i.e., gum, candy, etc) and if there is, to remove it.
2. Ask patient about the current condition of his/her teeth. Ask patient if he/she wears dentures. Do teeth or dentures bother patient now?
3. Ask patient whether he/she notices any movements in mouth, face, hands, or feet. If yes, ask to describe and to what extent they currently bother patient or interfere with his/her activities.
4. Have patient sit in chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at entire body for movements while in this position).
5. Ask patient to sit with hands hanging unsupported. If male, between legs, if female, and wearing a dress, hanging over knees. (Observe hands and other body areas.)
6. Ask patient to open mouth. (Observe tongue at rest within mouth.) Do this twice.
7. Ask patient to protrude tongue. (Observe abnormalities of tongue movement.)
8. **Ask patient to tap thumb, with each finger, as rapidly as possible for 10-15 seconds: separately with right hand, then with left hand. (Observe facial and leg movements.)
9. Flex and extend patient's left and right arms, one at a time. (Note any rigidity and rate it.)
10. Ask patient to stand up. (Observe in profile. Observe all body areas again, hips included.)
11. **Ask patient to extend both arms outstretched in front with palms down. (Observe trunk, legs, and mouth.)
12. **Have patient walk a few paces, turn, and walk back to chair. (Observe hands and gait.) Do this twice.

**Activated movements.

SANTA CLARA COUNTY MENTAL HEALTH

Confidential Patient Information
See Welfare & Institution Code 5328

<p>Patient Name _____ (Last, First, MI) Unicare # _____ Provider _____</p>

ABNORMAL INVOLUNTARY MOVEMENT SCALE (AIMS)

Instructions: Complete Examination Procedure before making ratings.

Code: 0=None, 1=Minimal, may be extreme normal, 2=Mild, 3=Moderate, 4=Severe

MOVEMENT RATINGS: Rate highest severity observed. Rate movements that occur upon activation one less than those observed spontaneously. Circle movement as well as code number that applies.		
Facial and oral movements	1. Muscles of Facial Expression e.g. Movements of forehead, eyebrows, periorbital area, cheeks, including frowning, blinking, smiling, and grimacing.	0 1 2 3 4
	2. Lips and Perioral Area e.g. puckering, pouting, smacking	0 1 2 3 4
	3. Jaw e.g. biting, clenching, chewing, mouth opening, lateral movement	0 1 2 3 4
	4. Tongue Rate only increases in movement both in and out of mouth. NOT inability to sustain movement. Darting in and out of mouth.	0 1 2 3 4
Extremity Movements	5. Upper (arms, wrists, hands, fingers) Include choreic movements (e.g. rapid, objectively purposeless, irregular, complex, serpentine). DO NOT INCLUDE TREMOR (e.g. repetitive, regular, rhythmic)	0 1 2 3 4
	6. Lower (legs, knees, ankles, toes) e.g. lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot.	0 1 2 3 4
Trunk Movements	7. Neck, shoulders, hip e.g. rocking, twisting, squirming, pelvic gyrations	0 1 2 3 4
Global Judgments	8. Severity of abnormal movements overall	0 1 2 3 4
	9. Incapacitation due to abnormal movements	0 1 2 3 4
	10. Patient's awareness of abnormal movements 0=No awareness, 1=Aware, no distress, 2=Aware, mild distress, 3=Aware, moderate distress, 4=Aware, severe distress	0 1 2 3 4
Dental Status	11. Current problems with teeth and/or dentures	No Yes
	12. Are dentures usually worn?	No Yes
	13. Edentia?	No Yes
	14. If known, do movements disappear in sleep?	No Yes NA

Doctor Signature: _____

Date: _____

Name: _____

Date: _____

Barnes Akathisia Rating Scale (BARS)

Instructions: Patient should be observed while they are seated, and then standing while engaged in neutral conversation (for a minimum of two minutes in each position). Symptoms observed in other situations, for example while engaged in activity on the ward, may also be rated. Subsequently, the subjective phenomena should be elicited by direct questioning.

Objective

- 0 Normal, occasional fidgety movements of the limbs
- 1 Presence of characteristic restless movements: shuffling or tramping movements of the legs/feet, or swinging of one leg while sitting, *and/or* rocking from foot to foot or "walking on the spot" when standing, but movements present for less than half the time observed
- 2 Observed phenomena, as described in (1) above, which are present for at least half the observation period
- 3 Patient is constantly engaged in characteristic restless movements, *and/or* has the inability to remain seated or standing without walking or pacing, during the time observed

Subjective

Awareness of restlessness

- 0 Absence of inner restlessness
- 1 Non-specific sense of inner restlessness
- 2 The patient is aware of an inability to keep the legs still, or a desire to move the legs, *and/or* complains of inner restlessness aggravated specifically by being required to stand still
- 3 Awareness of intense compulsion to move most of the time *and/or* reports strong desire to walk or pace most of the time

Distress related to restlessness

- 0 No distress
- 1 Mild
- 2 Moderate
- 3 Severe

Global Clinical Assessment of Akathisia

- 0 *Absent.* No evidence of awareness of restlessness. Observation of characteristic movements of akathisia in the absence of a subjective report of inner restlessness or compulsive desire to move the legs should be classified as pseudoakathisia
- 1 *Questionable.* Non-specific inner tension and fidgety movements
- 2 *Mild akathisia.* Awareness of restlessness in the legs *and/or* inner restlessness worse when required to stand still. Fidgety movements present, but characteristic restless movements of akathisia not necessarily observed. Condition causes little or no distress.
- 3 *Moderate akathisia.* Awareness of restlessness as described for mild akathisia above, combined with characteristic restless movements such as rocking from foot to foot when standing. Patient finds the condition distressing
- 4 *Marked akathisia.* Subjective experience of restlessness includes a compulsive desire to walk or pace. However, the patient is able to remain seated for at least five minutes. The condition is obviously distressing.
- 5 *Severe akathisia.* The patient reports a strong compulsion to pace up and down most of the time. Unable to sit or lie down for more than a few minutes. Constant restlessness which is associated with intense distress and insomnia.

Scoring the Barnes Akathisia Rating Scale (BARS)

The Barnes Akathisia Rating Scale is scored as follows:

Objective Akathisia, Subjective Awareness of Restlessness and Subjective Distress Related to Restlessness are rated on a 4-point scale from 0 – 3 and are summed yielding a total score ranging from 0 to 9.

The Global Clinical Assessment of Akathisia uses a 5-point scale ranging from 0 – 4.

Citation: Barnes TR. A rating scale for drug-induced akathisia. *British Journal of Psychiatry* 1989;154(5):672-676.
This scale can be reproduced freely.

Patient Name: _____ Rater Name and Date: _____

MODIFIED SIMPSON-ANGUS SCALE (MSAS)

Extrapyramidal Side Effects Scale

Each item is rated on a 5-point scale of severity (0 = normal; 4 = most severe; NR = not rated). Circle the rating that best describes the subject's present condition (3 is upper limit for patients without EPS).

1. Gait: The patient is examined as he walks into the examining room: his gait, the swing of his arms, his general posture all form the basis for an overall score for this item. This is rated as follows:

- 0 = Normal
- 1 = Diminution in swing while the subject is walking
- 2 = Marked diminution in swing with obvious rigidity in the arm
- 3 = Stiff gait with arms held rigidly before the abdomen
- 4 = Stooped, shuffling gait with propulsion and retropulsion
- NR = Not ratable

2. Arm Dropping: The patient and the examiner both raise their arms to shoulder height and let them fall to their sides. In a normal subject, a stout slap is heard as the arms hit the sides. In the patient with extreme Parkinson's Syndrome, the arms fall very slowly.

- 0 = Normal, free fall with loud slap and rebound
- 1 = Fall slowed slightly with less audible contact and little rebound
- 2 = Fall slowed, no rebound
- 3 = Marked slowing, no slap at all
- 4 = Arms fall as though against resistance, as though through glue
- NR = Not ratable

3. Shoulder Shaking: The subject's arms are bent at a right angle at the elbow and are taken one at a time by the examiner, who also grasps one hand and also clasps the other around the subject's elbow. The subject's upper arm is pushed to and fro, and the humerus is externally rotated. The degree of resistance from normal to extreme rigidity is scored as follows:

- 0 = Normal
- 1 = Slight stiffness and resistance
- 2 = Moderate stiffness and resistance
- 3 = Marked rigidity with difficulty in passive movement
- 4 = Extreme stiffness and rigidity with almost a frozen joint
- NR = Not ratable

4. Elbow Rigidity: The elbow joints are separately bent at right angles and passively extended and flexed, with the subject's biceps observed and simultaneously palpated. The resistance to this procedure is rated. (The presence of cogwheel rigidity is noted overall but not rated as a separate item.)

- 0 = Normal
- 1 = Slight stiffness and resistance
- 2 = Moderate stiffness and resistance
- 3 = Marked rigidity with difficulty in passive movement
- 4 = Extreme stiffness and rigidity with almost a frozen joint
- NR = Not ratable

5. Wrist Rigidity or Fixation of Position: The wrist is held in one hand and the fingers held by the examiner's other hand, with the wrist moved to extension, flexion, and ulnar and radial deviation, or the extended wrist is allowed to fall under its own weight, or the arm can be grasped above the wrist and shaken to and fro. A "1" score would be a hand that extends easily, falls loosely, or flaps easily upwards and downwards.

- 0 = Normal
- 1 = Slight stiffness and resistance
- 2 = Moderate stiffness and resistance
- 3 = Marked rigidity with difficulty in passive movement
- 4 = Extreme stiffness and rigidity with almost a frozen joint
- NR = Not ratable

6. Head Rotation: The subject sits or stands and is told that the examiner will move his head from side to side, that it will not hurt, and that he should try and relax. (Questions about pain in the cervical area or difficulty in moving his head should be obtained to avoid causing any pain.) Clasp the subject's head between the two hands with the fingers on the back of the neck. Gently rotate the head in a circular motion 3 times and evaluate the muscular resistance to this movement.

- 0 = Loose, no resistance
- 1 = Slight resistance to movement
- 2 = Resistance is apparent and the time of rotation is shortened
- 3 = Resistance is obvious and rotation is slowed
- 4 = Head appears stiff and rotation is difficult to carry out
- NR = Not ratable

Patient Name: _____

Rater Name and Date: _____

7. Glabella Tap: The subject is told to open his eyes and not to blink. The glabella region is tapped at a steady, rapid speed. Note the number of times that the subject blinks in succession. Take care to stand behind the subject so that he does not observe the movement of the tapping finger. A full blink need not be observed; there may be a contraction of the infraorbital muscle producing a twitch each time a stimulus is delivered. Vary the speed of tapping to assure that the muscle contraction is related to the tap.

- 0 = 0 to 5 blinks
- 1 = 6 to 10 blinks
- 2 = 11 to 15 blinks
- 3 = 16 to 20 blinks
- 4 = 21 or more blinks
- NR = Not ratable

8. Tremor: The subject is observed walking into the examining room and then is re-examined for this item with his arms extended at right angles to the body and the fingers spread out as far as possible.

- 0 = Normal
- 1 = Mild finger tremor, obvious to sight and touch
- 2 = Tremor of hand or arm occurring spasmodically
- 3 = Persistent tremor of one or more limbs
- 4 = Whole body tremor
- NR = Not ratable

9. Salivation: The subject is observed while talking and then asked to open his mouth to elevate his tongue.

- 0 = Normal
- 1 = Excess salivation so that drooling takes place if mouth is opened and tongue is raised
- 2 = Excess salivation is present and might occasionally result in difficulty in speaking
- 3 = Speaking with difficulty because of excess drooling
- 4 = Frank drooling
- NR = Not ratable

10. Akathisia: The subject is observed for restlessness. If restlessness is noted, ask, "Do you feel restless or jittery inside; is it difficult to sit still?" Subjective response is not necessary for scoring, but subject report can help make the assessment.

- 0 = No restlessness reported or observed
- 1 = Mild restlessness observed, e.g., occasional jiggling of the foot occurs when the subject is seated
- 2 = Moderate restlessness observed, e.g., on several occasions, the subject jiggles his foot, crosses and uncrosses his legs, or twists a part of the body
- 3 = Restlessness is frequently observed, e.g., the subject's foot or legs are moving most of the time
- 4 = Restlessness persistently observed, e.g., the subject cannot sit still, might get up and walk
- NR = Not ratable

TOTAL SCORE: _____

Total Score Severity:

- Less than 3 = normal
- 3 to 5 = minimal degree of movement disorder
- 6 to 11 = clinically significant degree of movement disorder
- 12 to 17 = severe degree of movement disorder is present

References:

Simpson GM, Angus JWS. A rating scale for extrapyramidal side effects. Acta Psychiatrica Scandinavica 1970;212(Suppl 44): 11-19.

Hawley CJ, Finneberg N, Roberts AG, Baldwin D, Sahadevan A, Sharman V. The use of the Simpson Angus Scale for the assessment of movement disorder: A training guide. Int J Psych Clin Pract 2003; 7: 249-257.

Rush J (2000) Handbook of Psychiatric Measures. Washington: American Psychiatric Publishing.