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Mexiletine Regime in Headache

Patient Information

Mexiletine belongs to a class of drugs called anti-arrhythmic which have been used to treat irregular heartbeat (arrhythmia). Some studies indicate that it is useful in treating pain syndromes. Use the following schedule to gradually increase your dose of Mexiletine. You should continue to increase the dose until it is effective at suppressing your attacks or side effects become evident. If you start to get any side effects, please let your General Practitioner or Neurologist know as soon as possible. Do not exceed the maximum dose of 400mg three times daily.

	Morning	**Midday**	**Evening**
For 7 days take:			**200mg**
For 7 days take:	**200mg**		**200mg**
For 7 days take:	**200mg**	**200mg**	**200mg**
For 7 days take:	**200mg**	**200mg**	**400mg**
For 7 days take:	**200mg**	**400mg**	**400mg**
Thereafter take:	**400mg**	**400mg**	**400mg**

• When This Medication Should Not Be Used

- If you have ever had an allergic reaction to Mexiletine, Lidocaine or Tocainide
- If you have a heart disorder, liver disease or seizures

• How To Use This Medication:

- Do not use more medicine or use it more often than you doctor tells you to
- May be taken with food, milk or antacids to avoid stomach upset
- You may need to carry identification to let others know you are using Mexiletine

• If A Dose Is Missed

- If you miss a dose, take your medicine as soon as possible if you are less than 4 hour late
- Otherwise, skip the missed dose and go back to your regular dosing schedule
- You should not use two doses at the same time

• How To Store And Dispose Of This Medication:

- Store at room temperature, away from heat and moisture and direct sunlight
- Keep all medicine out of the reach of children

• Drugs And Food To Avoid:

- Ask you doctor or pharmacist before using any other medicine, including over-the-counter medicine, vitamins, and herbal products
- Tell your doctor if you are also using phenytoin (Epanutin) or other heart medicines such as lidocaine or digoxin
- Do not smoke while using this medicine
- Try to limit the amount of caffeine you use because mexiletine decreases your body's ability to breakdown and eliminate caffeine

• Warnings While Using This Medicine:

- Make sure you doctor knows if you are pregnant or breastfeeding, or if you have heart disease, liver disease, seizures or low blood pressure
- Tell your doctor or dentist that you are using Mexiletine before having any kind of surgery
- Do not suddenly stop using this medicine without asking you doctor
- Mexiletine may make you dizzy or drowsy. Be careful if you drive a car or operate machinery

• Possible Side Effect While Using This Medicine:

- Call your doctor right away if you notice any of these side effects:
  - Irregular heart beat
  - Chest pain
  - Shortness of breath or trouble breathing
  - Skin rash, sever itching or hive
- If you notice these less serious side effects, talk with your doctor:
  - Dizziness, light-headedness or nervousness
  - Nausea, vomiting, or upset stomach
  - Diarrhoea or constipation
  - Trembling or shaking of hands
  - Blurred vision, tiredness or weakness
- If you notice other side effects that you think are caused by this medicine, tell your doctor

References

1. "Mexilietine."In DRUGDEX® System. Thomson Micromedex. http://www.thomsonhc.com (accessed December 10, 2005).
2. Tremont-Lukats, I. W., V. Challapalli, et al. (2005). "Systemic administration of local anesthetics to relieve neuropathic pain: a systematic review and meta-analysis." Anesth Analg 101(6): 1738-49.
3. Jarvis, B. and A. J. Coukell (1998). "Mexiletine. A review of its therapeutic use in painful diabetic neuropathy." Drugs 56(4): 691707.
4. Challapalli, V., I. W. Tremont-Lukats, et al. (2005). "Systemic administration of local anesthetic agents to relieve neuropathic pain." Cochrane Database Svst Rev(4): CD003345.

Mexiletine in Headache

Physician Information

• Contraindications

- Cardiogenic shock
- Allergy or hypersensitivity to Mexiletine, Lidocaine or Tocainide
- Second- or third-degree AV block

• Precautions

- Alterations in defibrillation thresholds in patients with implantable cardioverter defibrillators
- Alterations in urinary pH (alkalization of the urine can prolong the half-life)
- Blood dyscrasias
- Congestive heart failure
- Electrolyte abnormalities (ie, hypokalemia)
- Hypotension
- Liver disease
- Mexiletine should not be used in postmyocardial infarction patients with asymptomatic or minimally symptomatic non-life threatening ventricular arrhythmias (increased mortality)
- Parkinson's disease (prominent side effect is tremors)
- Proarrhythmic events; new or worsened arrhythmias
- Seizure disorders
- Severe renal impairment
- Asymptomatic ventricular premature contractions
- Pregnancy or breastfeeding

• Medical evaluation

- Initial evaluation:
  - Baseline blood pressure, heart rate, and respiratory rate
  - Baseline general physical exam
  - Baseline liver function, electrolytes, FBC and renal studies
  - Baseline ECG
- Toxicity
  - Serum concentrations greater than 2 micrograms/milliliter (mcg/mL)
  - ECG findings: widening of QRS complexs, atrioventricular dissociation, atrial fibrillation, ventricular fibrillation, sinus bradycardia, Torsade de pointes

• Dosing Recommendations

- Effective doses range between 300mg/day to 1200mg/day
- Dosing higher than 1200mg is usually limited by CNS side effects
- Mean maximal tolerated dose 750mg/day
- There is not a correlation between plasma concentration and clinical effect of Mexiletine
- There is no statistically significant difference between conventional Mexiletine and Sustained release Mexiletine
- Symptom control:
  - Co-administration with cimetidine (300mg every 6 hours) may reduce the gastrointestinal effects without affecting plasma drug levels. Should first attempt Mexiletine dosing with food, milk or antacid
  - Advise patients to avoid caffeine, as Mexiletine decreases elimination
  - Advise patients to avoid smoking as it induces Mexiletine metabolism

Adverse Reactions

- Cardiovascular
  - Atrial arrhythmia (0.1%)
  - Palpitations (4.3% to 7.5%)
  - Chest pain (2.6% to 7.5%)
  - Bradycardia (0.4% to 1.7%)
  - Angina (0.3 to 1.7%)
  - Congestive heart failure (1%)
  - Oedema (0.2%)
  - Hypertension (0.1 %)
  - Hypotension (0.6%)
- Dermatologic
  - Alopecia (0.4%)
  - Rash (4%)
- Gastrointestinal
  - Peptic ulcer (0.08%)
  - Oesophageal Ulceration (0.01%)
  - Nausea, vomiting, heartburn (39%)
  - Diarrhea (5.2%)
  - Constipation (4.0%)
  - Appetite change (2.6%)
  - Abdominal pain or cramping (1.2%)
  - Dysphagia (0.2%)
  - Dry mouth (3%)
- Hematologic
  - Agranulocytosis (0.06% to 0.1%)
  - Leukopenia (0.06%)
  - Neutropenia (0.1%)
  - Thrombocytopenia (0.16%)
- Hepatic
  - Elevated liver function tests (1% to 2%)
- Immunologic
  - Systemic Lupus Erythematosus (0.04%)
- Musculoskeletal
  - Arthralgia (1.7%)
  - Myelofibrosis (0.02%)
- Neurologic (50%)
  - Dizziness or light headedness (18.9%)
  - Tremor (13%)
  - Ataxia (9.7%)
  - Changes in sleep habits (7.1 %)
  - Weakness (5%)
  - Anxiety (5%)
  - Fatigue (3.8%)
  - Speech difficulties (2.6%)
  - Confusion (2.6%)
  - Paresthesia, numbness, tinnitus, depression (2.4%)
  - Memory loss (0.9%)
  - Seizure (0.2%)
  - Loss of consciousness (0.06%)
- Ophthalmic
  - Blurred vision, nystagmus, diplopia (6%)
- Psychiatric
  - Hallucinations, depression, other psychological changes (0.3%)
  - Psychosis (0.2%)
- Renal
  - Urinary hesitancy/retention (0.2%)
- Reproductive
  - Impotence (0.4%)
- Respiratory
  - Dyspnea (3%)
  - Pulmonary fibrosis (case reports)

Drug Interactions

- Mexiletine inhibits the metabolism or elimination of:
  - Theophylline
  - Metoprolol
  - Disopyramide
  - Tizanidine
  - Caffeine
- Mexiletine metabolism is induced by:
  - Phenytoin
  - Fosphenytoin
  - Rifampin
  - Ritinavir
  - Smoking
- Mexiletine metabolism is decreased by:
  - Fluvoxamine
  - Propafenone
  - Quinidine

References

1. "Mexilietine."In DRUGDEX® System. Thomson Micromedex. http://www.thomsonhc.com (accessed December 10, 2005).
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