Patients requiring doses above 50 mg per day should be genotyped for the drug metabolizing enzyme CYP2D6 to determine if they are extensive metabolizers (EMs) or intermediate metabolizers (IMs) of CYP2D6. Genotyped patients who are identified as EMs or IMs, who need doses of greater than 50 mg per day, should be titrated to their maximum recommended human dose (MRHD) of 100 mg daily (see Warnings and Precautions 5.12). Patients who require doses of tetrabenazine greater than 50 mg per day, should be first tested and genotyped to determine if they are extensive or intermediate metabolizers (EMs or IMs) of CYP2D6. Tetrabenazine can cause parkinsonism. In a 12-week, double-blind, placebo-controlled study in patients with chorea associated with Huntington's disease, akathisia, parkinsonism, depression, insomnia, anxiety or sedation occurred in 33% of patients treated with tetrabenazine compared to 0% of placebo-treated patients (see Table 1). Other side effects such as reduced appetite, constipation, weight loss, skin rash, headache and dizziness were also observed in these studies. Individualization of dose with careful weekly titration is required. The 1 week's starting dose is 12.5 mg daily; 2 week, 25 mg daily; 3 week, 50 mg daily; 4 week, 75 mg daily; 5 week, 100 mg daily; 6 week, 125 mg daily; 7 week, 150 mg daily; 8 week, 200 mg daily. The maintenance dose is the lowest dose that is required to achieve clinical benefit. In the tapering phase of treatment, before discontinuation of tetrabenazine tablets, doses may be decreased by 25 mg every 1 to 2 weeks. In a 26-week, double-blind, placebo-controlled study in patients with chorea associated with Huntington's disease, tetrabenazine (125 mg daily) was associated with a significant improvement in total chorea score on the Unified Huntington's Disease Rating Scale (UHDRS) chorea subscore compared with placebo (see Table 1). The greatest improvement was observed between 4 and 8 week of treatment. Tetrabenazine can cause sedation, which is increased in frequency in Huntington's disease. Tetrabenazine tablets are contraindicated in patients with a history of depression or prior suicide attempts or inadequately treated depression (4, 5.2). Tetrabenazine can cause sedation, which is increased in frequency in Huntington's disease. Tetrabenazine tablets are contraindicated in patients with a history of depression or prior suicide attempts or inadequately treated depression (4, 5.2).
Tetrabenazine Tablets

Indication:
Tetrabenazine is indicated for the treatment of adults with Huntington's disease (HD).

Dosage and Administration:
- Patients should be started on a 2.5 mg/day dose and titrated upward to a maximum of 22.5 mg/day. The starting dose of tetrabenazine should be given once daily in the evening.
- Tetrabenazine should be continued at the same dose for at least 2 months before any dose change is considered.
- The maintenance dose should be tapered to 2.5 mg/day before discontinuation.

GI effects:
- Nausea and vomiting may occur.
- The incidence of these effects increased after the second dose titration period.
- This is not manifest in children younger than 12 years of age.

Other side effects:
- Sedation, akathisia, parkinsonism, depression, and difficulty swallowing.
- Increased coughing.
- Increased sweating.
- Increased salivation.
- Increased talking.

Warnings and Precautions:
- Risk of Suicidality: Inform patients and their families that tetrabenazine may cause depression or may worsen pre-existing depression. Encourage their families to remain alert to the emergence of suicidal ideation and to report it immediately to the patient's physician.
- Risk of tardive dyskinesia (TD).
- The risk of TD increases with longer duration of treatment and higher cumulative dose.
- Concomitant medications that can cause TD may increase the risk of TD with tetrabenazine tablets.
- Tetrabenazine tablets may increase the chance that you will have trouble swallowing. Increased coughing may occur. Tetrabenazine tablets increase your chance of having certain changes in the electrical activity in your muscles. Changes in the electrical activity in your muscles may occur in the tongue, mouth, face, and neck.
- Tetrabenazine tablets may cause you to have problems thinking. You may get a condition where you feel a strong urge to move. This is called akathisia.
- Tetrabenazine tablets increase the chance that you will have high fever.
- Tetrabenazine tablets may increase the chance that you will develop a high fever.
- High fever may cause serious side effects, including:
- Heart attack
- Stroke
- Weakness
- Muscle pain
- Irritability
- Nausea
- Vomiting
- Fast heart rate
- watery diarrhea
- Strained urination
- Seizures

Contraindications:
- Tetrabenazine tablets are contraindicated in patients with a history of a psychiatric disorder that is known to be associated with akathisia.
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Precautions:
- Tetrabenazine tablets may cause you to have problems thinking. You may get a condition where you feel a strong urge to move. This is called akathisia.
- Tetrabenazine tablets increase the chance that you may have trouble swallowing. Increased coughing may occur.
- Tetrabenazine tablets increase your chance of having certain changes in the electrical activity in your muscles. Changes in the electrical activity in your muscles may occur in the tongue, mouth, face, and neck.
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- Tetrabenazine tablets increase the chance that you may have trouble swallowing. Increased coughing may occur.
- Tetrabenazine tablets increase your chance of having certain changes in the electrical activity in your muscles. Changes in the electrical activity in your muscles may occur in the tongue, mouth, face, and neck.

Adverse Reactions:
- The most common adverse reactions were:
- nausea
- vomiting
- constipation
- dry mouth
- dizziness
- tremor
- abnormal movements
- depression
- akathisia
- sedation

Special populations:
- Children and adolescents: The safety and effectiveness of tetrabenazine tablets in children and adolescents have not been established.
- Elderly patients: Tetrabenazine tablets may cause increases in tremor and rigidity in elderly patients.

Other information:
- The cumulative percentage of patients with specified changes from baseline in total chorea score is shown in Figure 2.
- The probability of remission of chorea at 24 weeks was 97% in the placebo group and 91% in the tetrabenazine group.

References:
- The information in this Medication Guide was reviewed by the U.S. Food and Drug Administration.