

a TSA medical publication

# A Consumer's Guide to Tourette Syndrome Medications

by Gerald Erenberg, M.D.

Tourette Syndrome (TS) or Tourette's disorder (DSM IV-TR) is a complex neurobehavioral disorder characterized by a changing pattern of motor and vocal tics which begins in childhood. Diagnostic criteria indicate that symptoms should last for more than a year.

A number of individuals with Tourette Syndrome have associated behavioral problems such as attention deficit, obsessions, compulsions, impulsivity, irritability, aggression, anxiety, depression, and in rare cases, self-injurious behaviors. Some of these problems may or may not be an integral part of Tourette Syndrome, but others may be reactions to social stresses associated with coping with a chronic disorder. Other problems may include difficulties in processing information and learning. The challenge of coping with tics, behavioral problems, and learning disabilities can often lead to poor performance in school, in the work place and difficulty with social adjustment.

While most people feel a sense of relief at learning that there is a name and a medical reason for their TS symptoms, it may still take time to adjust to the consequences of a diagnosis. Moreover, TS affects individuals to varying degrees, depending on the age of the person, the presence or absence of other conditions or impairments, and the overall functioning of the individual. Today, there is much more information available about TS than even ten years ago, and the social and medical supports available are extremely important in adjusting to the new situation. Everyone who is important to the individual with TS should learn as much as they can about the disorder, including family, neighbors, teachers, camp counselors and, when possible, employers.

## does everyone with TS need medications?

Improved understanding about TS is often sufficient to help individuals adapt and cope with their problems without the use of medication. In fact, not all individuals with TS require medications. For example, young children may have very frequent tics, but due to a lack of awareness or impairment, often do not require any medication. On the other hand, adolescents with a less severe number of tics may ask for therapy because of the effect of even small numbers of tics on social or school functioning. Many individuals can function quite well with the help and support of family members, medical professionals and understanding educators and employers. However, when symptoms cause either significant impairment or distress, medication should be considered.

## general principles of medication treatment

At present there is no cure for Tourette Syndrome or for that matter any other tic disorder. Unfortunately, there is as yet no “perfect” medication for the treatment of this disorder.

If there were a perfect medication, it would:

- Be effective for all persons who take it;
- Completely eliminate the target symptoms;
- Never cause side effects, and
- Lead to a cure of the problems so that the medication could be stopped after a short time.

However, current medications available for the treatment of TS suffer from a number of limitations:

- Not all patients with TS respond to medications;
- Currently available medications for TS may only partially eliminate target symptoms;
- Side effects of medications are commonly experienced, and
- So far, no cure has been found for TS.

Moreover, there is no evidence that the early use of medication has any effect on the long-term course of the disorder. The leading theory today about the cause of TS is that it results from a chemical imbalance in the brain involving neurotransmitters. Neurotransmitters are chemicals within individual brain cells that are important in the transmission of messages between one brain cell and another. The neurotransmitter dopamine is most strongly associated with tics, but there are likely other such chemicals (serotonin and norepinephrine, for example) involved in causing other symptoms of TS. The medications available to reduce tic symptoms or the associated behavioral problems are believed to be beneficial because they may regulate the activity of several neurotransmitters.

In spite of the limitations, medications are often prescribed for target symptoms of TS. Furthermore, since there are no perfect medications for TS, the improvement seen may be somewhat limited. Because each of the currently available medications has potential short or long-term side effects, decisions about whether or not to treat TS symptoms with medication must take these realities into account, and a balance must be struck between the beneficial effects and the potential side effects. When medications are begun, dosages should be low to evaluate carefully the sensitivity of that individual toward a particular medication and its side effects. Low dosages should be followed by periodic increases to determine the optimal dosage for each individual.

Medications are metabolized or broken down by a system of enzymes in the liver and then distributed to the brain where they produce their active effects. Today, there is a considerable amount of information about these enzymes, known as the CYP450 system. Approximately 5-10% of Caucasians have alterations in this system, and therefore cannot easily break down certain medications. These individuals will be very sensitive to even small doses of

the medications used to control obsessive-compulsive symptoms or attentional problems. Certain combinations of medications may alter activity in this enzyme system, resulting in increased levels of those medications and the potential for adverse interactions. Thus, it is not always easy to predict how a person will respond to a given medication.

It is extremely important that individuals beginning medication report both the benefits and side effects they feel to their physicians so that together they can decide whether it is reasonable to try higher doses. Remember, medications may not begin to show effect immediately. Trials of weeks or even months may be needed before a final dosage can be determined. Medication should be continued only if the benefits clearly outweigh the side effects. Medication that relieves symptoms but causes major discomfort should be discontinued.

If a decision is reached that a medication is not helpful or is causing too many side effects, it should *not* be stopped abruptly, but instead reduced slowly and then stopped. There is always some risk that the sudden withdrawal of a medication can lead to adverse reactions. Your doctor will prescribe a step-by-step program of decreasing dosage until it is discontinued completely.

Drug holidays are periods of time, often in summer when, even though they have been found to be helpful, medications are purposely discontinued to re-evaluate their role. Tics and other symptoms wax and wane, and may diminish over time even without treatment. There is no strong evidence that medication holidays provide any long-term benefit, and it has been demonstrated that at least in some cases, staying on medications while symptoms are minimal may actually delay the onset of a worsening. Medications should be discontinued only at times when they are judged no longer necessary. They do not need to be stopped simply to fulfill the goal of having the individual off medication for some part of the year.

## which medication to use?

There is no single medication which is helpful to all individuals simply because a diagnosis of Tourette Syndrome has been made. Instead, patients and their physicians should discuss which symptoms are to be targeted for medication treatment. The medications commonly used to treat symptoms of

TS are reviewed in the tables on page 5. They are listed by general purpose, typical starting doses, common maximum dosages and common side effects. Children generally require lower dosages of the same medications that are used for adults. For some, the goal of medication treatment will be to reduce tic severity and frequency. For others, the primary symptoms requiring treatment may be those of a behavioral nature, or the primary symptoms may include both tics and behavioral or emotional difficulties. Because of the need to assess the response to any and all of these potential problems, it is extremely important to maintain communication with the treating physician. This will allow the doctor to better understand how well symptoms are being addressed.

### More than one medication

When there is more than one symptom to treat, individuals often require the use of more than one medication at a time to control them. This approach is called *targeted combined pharmacotherapy*, referring to the careful, judicious use of more than one medication simultaneously. For example, an individual may be prescribed one medication to reduce tics and a second medication to reduce some of the behavioral or emotional problems. The combined use of Haldol (haloperidol) and Prozac (fluoxetine) is one example of a combination used to control both tics and obsessive compulsive behaviors. Another example is the combination of Catapres (clonidine) and Dexedrine (dextroamphetamine) to reduce both tics and symptoms of Attention Deficit Hyperactivity Disorder. Potential interactions between the different medications prescribed need to be kept in mind with this approach and must be discussed with your doctor.

### The neuroleptics

The neuroleptic medications, e.g. Haldol (haloperidol) and Orap (pimozide) may have side effects involving the motor system such as restlessness, muscle stiffness or slowness, or a much less common side effect known as tardive dyskinesia (TD). Symptoms of TD may begin with twitching movements of the face and mouth which may not disappear when the medication is discontinued. Some of these side effects of neuroleptic medication can be controlled by anticholinergic medications such as Artane (trihexyphenidyl) and Cogentin (benztropine). These may not need to be given routinely,



but they may be added to the neuroleptics at the beginning of treatment to prevent the development of the motor side effects. Later they may be discontinued.

### **TS medications are used for other conditions**

Many medications prescribed for Tourette Syndrome are often used to treat conditions other than TS. For instance, Catapres (clonidine), is used to control high blood pressure. Klonopin (clonazepam) is used in the treatment of seizures as well as for the control of tics. Nevertheless, these and other medications have been studied for the treatment of tics and have been found to be effective for some individuals with TS.

### **Are generics effective?**

Whether generic medications are as effective as brand name medication is a question that still needs to be studied. Some individuals switching to generics from brand name products have reported experiencing no problems, but others have found the generics to be less beneficial than the brand name products. It is important that individuals review this issue with their physicians when a medication program is being started.

### **Antidepressants, stimulants and ADHD**

The group known as tricyclic antidepressant medications are so named because they are used to treat clinical depression. For many years, however, it has also been shown that these medications can improve attention deficits as well as decrease anxiety, control mood swings and alleviate bed wetting. Because tricyclic antidepressants generally do not increase, and indeed may reduce tics, these medications are often given to children with tics and attention deficit hyperactivity disorder (ADHD). They serve to decrease distractibility and improve concentration. The more commonly used medications for ADHD are stimulants such as Ritalin (methylphenidate), Adderall (mixed amphetamine) and Dexedrine (dextroamphetamine). While effective for ADHD, these medications may cause an increase in tics in some patients with TS. Experience has shown, however, that these medications can often be taken safely by individuals with TS. For those with significant ADHD symptoms, a trial of stimulant medication may prove helpful.

### **SSRIs**

A class of medications often useful in treating TS is known as selective serotonin reuptake inhibitors (SSRIs) because they affect the serotonin neurotransmitter system. These medications are helpful in treating depression, anxiety, and obsessive compulsive behaviors. It has also been shown that augmenting an SSRI with a neuroleptic may improve the effectiveness of the SSRI, something of particular importance to patients with tics.

### **Other agents**

Some newer agents have been reported to be of benefit for TS, but clear and convincing information is still lacking. As an alternative to neuroleptics, a new class of "atypical" antipsychotics that are used for schizophrenia (risperidone, olanzapine, and quetiapine, for example) have been shown to be helpful in TS. However, studies to compare these agents to traditional neuroleptics have not been done, and there is often a problem with weight gain with these drugs that can limit their usefulness. On the other hand, it has been suggested that the risk of tardive dyskinesia is less with these agents than traditional neuroleptics. Some investigators have reported benefits with nicotine in the form of a patch or gum, or the agent mecamylamine, that acts in the brain similarly to nicotine. However, more comprehensive studies have failed to show any dramatic benefit for tics, and their use for other features of TS is still under study. Finally, agents such as baclofen (a muscle relaxant) and tizanidine (used to treat spasticity) may be helpful for tics, but await further evaluation.

### **To summarize**

As can be seen, there is no single TS "drug of choice." Therefore, a careful matching of the medication to the specific needs of the individual is critical. Because there are no medical tests that can predict which medication will work best, more than one medication may need to be tried before the best treatment program is found. Unfortunately, there are some individuals who either may not respond to any of the available medications, or may respond but experience intolerable side effects. After several trials, it is sometimes best to agree that the individual person is better off not taking medication at all.





## medications used in the treatment of co-morbid ADHD and TS

Name	Starting Dose	Daily Dose	Possible Side Effects
<b><u>Tricyclic Antidepressants:</u></b>			
imipramine <b>Tofranil™</b>	10-25mg	50-300mg	Dry mouth, blurred vision, constipation, fatigue, EKG changes, weight gain
desipramine <b>Norpramin™</b>	10-25mg	50-300mg	Same as imipramine
nortriptyline <b>Pamelor™</b>	10-25mg	50-150mg	Same as imipramine
<b><u>Stimulant Medications:</u></b>			
methylphenidate <b>Ritalin™</b>	2.5-10mg	10-60mg	Headache, stomach ache, appetite loss, insomnia, irritability, increased tics
amphetamine salts <b>Adderall™</b>	2.5-5mg	5-60mg	Same as methylphenidate
dextroamphetamine <b>Dexedrine™</b>	2.5-5mg	5-30mg	Same as methylphenidate

## medications used in the treatment of co-morbid OCD and TS

Name	Starting Dose	Daily Dose	Possible Side Effects
fluoxetine <b>Prozac™</b>	2.5-20mg	5-80mg	Restlessness, insomnia, gastrointestinal upset, sexual dysfunction
paroxetine <b>Paxil™</b>	5-10mg	10-60mg	Same as fluoxetine
clomipramine <b>Anafranil™</b>	25mg	50-200mg	Dry mouth, blurred vision, constipation, fatigue, EKG changes, weight gain
sertraline <b>Zoloft™</b>	12.5-25mg	75-300mg	Fatigue, insomnia, restlessness, weight gain, sexual dysfunction
fluvoxamine <b>Luvox™</b>	25mg	50-300mg	Same as fluoxetine
citalopram <b>Celexa™</b>	10mg	20-40mg	Same as fluoxetine

## medications used in the treatment of tics

Name	Starting Dose	Daily Dose	Possible Side Effects
haloperidol <b>Haldol™</b>	0.25-0.5mg	1-5mg	Fatigue, weight gain, muscle rigidity, motor restlessness, tardive dyskinesia, school phobias, photosensitivity, depression, cognitive dulling
pimozide <b>Orap™</b>	0.5-1mg	1-10mg	Same as haloperidol, EKG changes
fluphenazine <b>Prolixin™</b>	0.5-1.0mg	0.5-6mg	Same as haloperidol
risperidone <b>Risperdal™</b>	0.25-0.5mg	0.5-6mg	Same as haloperidol
clonidine <b>Catapres™</b>	0.025-0.05mg	0.1-0.40mg	Fatigue, dry mouth, irritability, dizziness, headache, insomnia, hypotension
clonidine patch <b>Catapres™ patch</b>	TTS-TTS1	TTS1-TTS3	Same as clonidine tablets, localized skin rash
clonazepam <b>Klonopin™</b>	0.025-0.5mg	0.5-3.0mg	Fatigue, irritability, dizziness, disinhibition
guanfacine <b>Tenex™</b>	0.25-0.5mg	0.5-3.0mg	Fatigue, irritability, hypotension, sleep disturbance

## final thoughts

TS symptoms range from mild to severe, and many individuals with this disorder never require medication treatment. For those who do, consultation with your physician is key because an individualized medication program will be necessary. When reporting about symptom changes to your physician, it is helpful to be quite specific about which aspects of TS symptoms have changed for the better or worse and which, if any, of the side effects may have occurred.

There are other medications for TS that are available although they are used less commonly. The research community is working actively to discover new and better treatment programs. Until that time, the currently available medications can be of help to many individuals with Tourette Syndrome.

## safety advisories

### **Pimozide (Orap) contraindicated with clarithromycin (Biaxin) and other macrolide antibiotics\***

The labeling for pimozide (Orap), approved for the treatment of Tourette's disorder, has been updated to contraindicate use of pimozide in patients receiving macrolide antibiotics such as clarithromycin, erythromycin, azithromycin, and dirithromycin. Two sudden deaths have been reported when clarithromycin was added to ongoing pimozide therapy.

Pimozide prolongs the QT interval of the electrocardiogram, an effect that is believed to predispose patients to fatal cardiac arrhythmias. Because of this, pimozide is not intended as a first-choice treatment for Tourette's disorder. Electrocardiogram monitoring is recommended, and the dose of pimozide should not exceed 10 mg daily. Pimozide is contraindicated with other drugs that prolong the QT interval.

A plausible explanation for the cases of sudden death with concomitant clarithromycin and pimozide is a metabolic interaction that leads to increased pimozide plasma concentrations and thus an increased risk of cardiac arrhythmia. The macrolide antibiotics are inhibitors of the metabolic enzyme cytochrome P450 3A. Preliminary *in vitro* data suggest that clarithromycin is capable of inhibiting the metabolism of pimozide, which appears to be a substrate for cytochrome P450 3A (Flockhart DA, Richard E. Woosley RL, et al. A metabolic interaction between clarithromycin and pimozide may result in cardiac toxicity. *Clin Pharmacol Ther.* 1996;59:189. Abstract).

\* Information excerpted from  
*FDA Medical Bulletin/October 1996*

A general notice from the manufacturer to physicians warns that the following medications should NOT be taken in conjunction with Orap:

- Macrolide antibiotics (e.g. clarithromycin, erythromycin, dirithromycin, troleandomycin)
- Azole antifungal agents (e.g. itraconazole, ketoconazole)
- Protease inhibitors (e.g. ritonavir, saquinavir, indinavir, nelfinavir)
- Nefazodone
- Zileuton

As a precaution, patients should also avoid grapefruit juice because it contains substances that may inhibit the metabolism of pimozide by CYP 3A.

If you have questions about this information, we urge you to contact your personal physician.

TSA has made every effort to consult with world-renowned experts in the development of this booklet. It is intended to provide information about medications currently in use for TS treatment. Readers are cautioned against taking and/or changing medications based on this information without first consulting a physician.

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I wish to thank the following colleagues for their valuable assistance in revising and updating this TSA publication:

Leon S. Dure, M.D. and Paul Sandor, M.D.

— G. E.

TSA gratefully acknowledges the counsel and guidance of its Medical Advisory Board in the review of this publication. Members of the TSA Medical Advisory Board welcome queries from colleagues and other professionals and can be reached by contacting the Tourette Syndrome Association, Inc.

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## additional TSA resources

### Videos & Vignettes

- AV-9 After the Diagnosis . . . The Next Steps**  
Produced expressly for individuals and families who have received a new diagnosis of TS. This video was developed to help clarify what TS is, to offer encouragement, and to dispel misperceptions about having TS. Features several families in excerpts from the *Family Life With TS A Six-Part Series* who recount their own experiences as well as comments from medical experts. Narrated by Academy Award Winner Richard Dreyfuss. 35 min.
- AV-10 The Complexities of TS Treatment: A Physicians' Roundtable**  
Three internationally recognized TS experts, Drs. Cathy Budman, Joseph Jankovic and John Walkup provide colleagues with valuable information about the complexities of treating and advising families with TS. Emphasis is on different clinical approaches to patients with a broad range of symptom severity. Co-morbid and associated conditions are covered. 15 min.
- AV-10a Clinical Counseling: Towards an Understanding of Tourette Syndrome**  
Targeted to counselors, social workers, educators, psychologists and families, this video features expert physicians, allied professionals and several families summarizing key issues that can arise when counseling families with TS. Includes valuable insights from the vantage point of those who have TS and those who seek to help them. 15 min.
- AV-11 Family Life With Tourette Syndrome . . . Personal Stories . . . A Six-Part Series**  
Adults, teenagers, children, and their families . . . all affected by Tourette Syndrome describe lives filled with triumphs and setbacks . . . struggle and growth. Informative and inspirational, these stories present universal issues and resonate with a sense of hope, possibility, and love. 58 min.

An up-to-date Catalog of Publications and Videos, can be obtained by contacting:

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