Sex offenders traditionally are managed by the criminal justice system, but psychiatrists are frequently called on to assess and treat these individuals. Part of the reason is the overlap of paraphilias (disorders of sexual preference) and sexual offending. Many sexual offenders do not meet DSM criteria for paraphilias, however, and individuals with paraphilias do not necessarily commit offenses or come into contact with the legal system.

As clinicians, we may need to assess and treat a wide range of sexual issues, from persons with paraphilias who are self-referred and have no legal involvement, to recurrent sexual offenders who are at a high risk of repeat offending. Successfully managing sex offenders includes psychological and pharmacologic interventions and possibly incarceration and post-incarceration surveillance. This article focuses on pharmacologic interventions for male sexual offenders.

Reducing sexual drive
Sex offending likely is the result of a complex interplay of environment and psychological and biologic factors. The biology of sexual function provides numerous targets for pharmacologic intervention, including:

- endocrine factors, such as testosterone
- neurotransmitters, such as serotonin.

The use of pharmacologic treatments for sex offenders is off-label, and evidence is limited. In general, pharmacologic treatments are geared toward reducing
sexual drive through nonhormonal or hormonal means (Table 1).3,5

### Nonhormonal treatments

**SSRIs.** Selective serotonin reuptake inhibitors act by blocking serotonin reuptake in the synaptic cleft. Soon after the first SSRIs were approved in 1988, reports appeared of SSRIs interfering with sexual functioning.6 This side effect quickly was exploited to assist the treatment of sexual offenders.7

The mechanism of action may include:4

- direct effects, such as general inhibition of sexual activity, reduced impulsiveness, and an effect on the hypothesized “obsessive-compulsive” nature of paraphilias9
- indirect reduction of testosterone.

A growing body of literature supports SSRIs’ effectiveness in treating paraphilias and sexual offenders. Greenberg7 reviewed case studies and open drug trials of nearly 200 patients receiving fluoxetine, fluvoxamine, sertraline, or paroxetine. Eight studies showed benefits; however, Adi noted that this preliminary evidence was “far from conclusive.”

SSRIs generally are well tolerated and may be more appealing to patients than the “chemical castration” of hormonal treatments. Dosing is similar to that used in depression or obsessive-compulsive disorder. Although most patients notice beneficial effects in 2 to 4 weeks, some notice the effect nearly immediately.

**Naltrexone.** An opioid antagonist thought to affect the CNS processes of pleasure and pain, naltrexone has been used to treat alcohol dependence and pathologic gambling. A few case studies10-14 and 1 study of 21 adolescent sex offenders15 have shown benefits in treating sexual offenders or paraphiliacs. Benefits were seen at 50 mg/d,
INVEGA® (paliperidone) Extended-Release Tablets

subjects and younger subjects, and other reported clinical experience has not identified differences in response between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. This drug is known to be substantially excreted by the kidney and clearance is decreased in patients with moderate to severe renal impairment [see Clinical Pharmacology (12.3) in full PI], who should be given reduced doses. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function [see Dosage and Administration (2.5) in full PI].

Renal Impairment: Dosing must be individualized according to the patient’s renal function status [see Dosage and Administration (2.5) in full PI].

Hepatic Impairment: No dosage adjustment is required in patients with mild to moderate hepatic impairment. INVEGA® has not been studied in patients with severe hepatic impairment.

DRUG ABUSE AND DEPENDENCE

Controlled Substance: INVEGA® (paliperidone) is not a controlled substance.

Abuse: Paliperidone has not been systematically studied in animals or humans for its potential for abuse. It is not possible to predict the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed. Consequently, patients should be evaluated carefully for a history of drug abuse, and such patients should be observed closely for signs of INVEGA® misuse or abuse (e.g., development of tolerance, increases in dose, drug-seeking behavior).

Dependence: Paliperidone has not been systematically studied in animals or humans for its potential for tolerance or physical dependence.

OVERDOSAGE

Human Experience: While experience with paliperidone overdose is limited, among the few cases of overdose reported in pre-marketing trials, the highest estimated ingestion of INVEGA® was 405 mg. Observed signs and symptoms included extrapyramidal symptoms and gait unsteadiness. Other potential signs and symptoms include those resulting from an exaggeration of paliperidone’s known pharmacological effects, i.e., drowsiness and somnolence, tachycardia and hypotension, and QT prolongation.

Paliperidone is the major active metabolite of risperidone. Overdose experience reported with risperidone can be found in the OVERDOSAGE section of the risperidone package insert.

Management of Overdose: There is no specific antidote to paliperidone, therefore, appropriate supportive measures should be instituted and close medical supervision and monitoring should continue until the patient recovers. Consideration should be given to the extended-release nature of the product when assessing treatment needs and recovery. Multiple drug involvement should also be considered.

In case of acute overdose, establish and maintain an airway and ensure adequate oxygenation and ventilation. Gastric lavage (after intubation if patient is unconscious) and administration of activated charcoal together with a laxative should be considered.

The possibility of obtundation, seizures, or dystonic reaction of the head and neck following overdose may create a risk of aspiration with induced emesis. Cardiovacular monitoring should commence immediately, including continuous electrocardiographic monitoring for possible arrhythmias. If antarrhythmic therapy is administered, disopyramide, procainamide, and quinidine carry a theoretical hazard of additive QT-prolonging effects when administered in patients with an acute overdose of paliperidone. Similarly the alpha-blocking properties of bretylium might be additive to those of paliperidone, resulting in problematic hypotension.

Hypotension and circulatory collapse should be treated with appropriate measures, such as intravenous fluids and/or sympathomimetic agents (epinephrine and dopamine should not be used, since beta stimulation may worsen hypotension in the setting of paliperidone-induced alpha blockade). In cases of severe extrapyramidal symptoms, anticholinergic medication should be administered.

Inactive ingredients are carnauba wax, cellulose acetate, hydroxyethyl cellulose, propylene glycol, polyethylene glycol, polyethylene oxides, povidone, sodium chloride, stearic acid, butylated hydroxytoluene, hypromellose, titanium dioxide, and iron oxides. The 3 mg tablets also contain lactose monohydrate and triacetin.

Manufactured by:
ALZA Corporation, Vacaville, CA 95688 OR
Janssen Cilag Manufacturing, LLC, Gurabo, Puerto Rico 00778

Manufactured for:
Janssen, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc., Titusville, NJ 08560
OROS is a registered trademark of ALZA Corporation ©Ortho-McNeil-Janssen Pharmaceuticals, Inc. 2007 Revised: July 2009

101059858

continued from page 61

Table 2

Common side effects of antiandrogen therapy

<table>
<thead>
<tr>
<th>Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
</tr>
<tr>
<td>Fatigue</td>
</tr>
<tr>
<td>Gynecomastia</td>
</tr>
<tr>
<td>Hot flashes</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Low libido</td>
</tr>
<tr>
<td>Myalgia</td>
</tr>
<tr>
<td>Osteopenia</td>
</tr>
<tr>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Sweating</td>
</tr>
<tr>
<td>Thromboembolism</td>
</tr>
<tr>
<td>Weight gain</td>
</tr>
</tbody>
</table>

with suggested dosing of 100 to 200 mg/d. Because data are very limited, consider naltrexone only on an individual basis or as a possible adjunctive treatment.

Psychostimulants. Methylphenidate was added to augment SSRI treatment in a study of 26 men with paraphilias or paraphilia-related disorders. Results included further significant decreases in total sexual outlets (orgasms per week) and average time spent per day in paraphilia and paraphilia-related behavior. These gains appeared to be independent of the presence of attention-deficit/hyperactivity disorder.

Again, because data are very limited, consider this strategy only on an individual basis or as a possible adjunctive treatment. Because sexual offenders have high rates of substance abuse, consider the potential for stimulant abuse.

Hormonal treatments

Because testosterone is required for healthy bone metabolism, the antiandrogen medications used in hormonal treatment can cause osteoporosis. Therefore, long-term antiandrogen treatment should include bone scans to monitor for osteopenia and osteoporosis. Some authors have suggested that monthly doses of 25 to 50 mg of testosterone could minimize this risk. Bisphosphonates, vita-
min D, and calcium supplements at osteoporosis treatment levels might be helpful. Other common side effects of antiandrogen medications are listed in Table 2.

**Finasteride** is approved for treating benign prostatic hyperplasia and androgenetic alopecia. It works by preventing conversion of testosterone to dihydrotestosterone (DHT) by the type II isoenzyme. Serum DHT contributes to male sexual behavior and predicts frequency of orgasms in healthy volunteers. Although there have been no studies of finasteride in sex offenders, it may be more acceptable to patients than other hormonal treatments and have a theoretical benefit in reducing sexual drive. Clinically, some patients describe increased control over urges without substantial side effects. Because there is no evidence supporting finasteride use in sex offenders, consider this medication only on an individual basis or as a possible adjunctive treatment.

**Cyproterone acetate** (CPA) is a synthetic steroid that blocks androgen receptors. Some evidence supports its use in treating sex offenders, although this agent is not available in the United States. For more information about CPA, see this article at CurrentPsychiatry.com.

**Medroxyprogesterone acetate** (MPA), a derivative of progesterone, lowers serum testosterone by inhibiting its production through reducing pituitary luteinizing hormone (LH). The typical dose range for use in sex offenders is 100 to 600 mg/d orally or 100 to 700 mg IM every week, although some authors suggest giving similar doses every 2 weeks.

Side effects of MPA include hypersomnia; neurasthenia; weight gain; hot flashes; gynecomastia; increased scalp hair; and decreased erections, ejaculate volume, spermatogenesis, and body and facial hair. The drug decreases testosterone levels by about 50%. Positive effects include reduced interest in and energy spent on pursuing sexual goals, but preservation of nondeviant sexual arousal.

MPA has been shown to effectively decrease deviant sexual arousal and recidivism. In a study of 100 patients receiving MPA (average 250 mg IM every 2 weeks) for an average of 3 years, only 1 re-offended while taking MPA.

In a 5-year follow-up study of 275 men, subjects were classified into high risk/treatment with MPA, 200 to 400 mg IM every 2 weeks, and low risk/nontreatment groups. A portion of the high risk/treatment group did not receive MPA. No sexual re-offenses occurred among high-risk subjects who received MPA, whereas the recidivism rate was 18% among high-risk subjects who did not receive MPA. Subjects in the low risk/nontreatment group had a recidivism rate of 15%, which suggests the need for more liberal use of antiandrogens. One major confounding factor was that subjects in the high risk/treatment group had to report every 2 weeks for injections; this may have resulted in closer follow-up, monitoring, and support, which may have contributed to lower recidivism.

**Gonadotropin-releasing hormone (GNRH) agonists.** The terms gonadotropin-releasing hormone and luteinizing-releasing hormone are used interchangeably. Most body testosterone is produced and released by Leydig cells in the testes in response to stimulation by LH released by the pituitary gland. LH release is controlled by the pulsatile release of GNRH from the hypothalamus. GNRH agonists are high-potency analogs of GNRH that work by causing an initial surge of LH followed by down-regulation of gonadotroph cells, a drop in LH, and a drop in testosterone to castration levels.

The GNRH analogs leuprolide, goserelin, and triptorelin are used to treat paraphiliacs and sexual offenders. Leuprolide typically is dosed at 7.5 mg IM every month, 22.5 mg IM every 3 months, or 30 mg IM every 4 months. Goserelin is provided as a subcutaneous implant/depot injected as 3.6 mg every month or 10.8 mg every 3 months.

Triptorelin is FDA-approved as treatment for advanced prostate cancer. Triptorelin is given in depot formulation as
3.75 mg IM every month or in a long-acting form as 11.25 mg IM every 3 months.

When starting these medications, an initial surge of LH and testosterone can last up to 3 weeks.\textsuperscript{26} Theoretically, this could worsen paraphiliac interests. Many practitioners will use a testosterone blocker such as flutamide, 250 mg tid, for the initial weeks of treatment.

Side effects of the GNRH agonists are similar. Most patients initially experience hot flashes. A systemic literature review\textsuperscript{27} reported:
- weight gain
- perspiration
- gynecomastia
- urinary incontinence
- hot flashes
- decreased growth of facial and body hair
- asthenia
- erectile failure
- muscle tenderness
- frequent bone demineralization.

Rare cases of pituitary apoplexy (a clinical syndrome secondary to infarction of the pituitary gland) have been reported, possibly related to an underlying pituitary adenoma.\textsuperscript{28}

In a literature review that totalled 118 patients,\textsuperscript{27} GNRH agonists significantly decreased erections, ejaculations, paraphilic fantasies, and paraphilic behavior. Patients also reported feeling more relaxed, and recidivism rates were low. Some patients who failed to respond to CPA and MPA responded to GNRH agonists. Subsequent studies found similar results.\textsuperscript{29,30}

### Monitoring

**Laboratory investigations** are recommended to monitor for side effects of antiandrogen medications (Table 3).\textsuperscript{19,27,31} Medical contraindications to rule out before initiating antiandrogen medications include:

- thromboembolic diseases
- liver disease
- bone demineralization disorders
- hypersensitivity to the drug.

Measure prolactin to rule out pituitary adenomas. Monitor serum testosterone because some patients will not experience testosterone suppression from GNRH agonists or other antiandrogens. Noncompliant patients could potentially reverse the effects of MPA and GNRH agonists by taking exogenous testosterone.

### Medication selection

The goals of pharmacologic treatment of sex offenders are to:

- reduce sexual offending and victimization
- suppress sexual drive to a controllable level
- possibly preferentially eliminate deviant arousal/thoughts
- allow normal sexual relationships.

### Gauging risk

In determining which pharmacologic treatment to offer a patient, first evaluate the individual’s risk for recidivism. Actuarial scales\textsuperscript{32,33} suggest that recidivism risk can be categorized, based on clinical factors (Table 4).\textsuperscript{4,25,34}

In addition to statistical risk factors,
several other factors affect medication selection. Self-referred individuals may be more reliable in taking oral medications than those referred by the courts. A developmentally delayed individual may be a poor candidate for oral medication, unless he resides in a group home setting where compliance can be assured. Efficacy also guides medication choice. Finally, some patients will be legally required to provide proof of compliance, which only IM medications provide.

### Treatment

Based on clinical experience and available literature, Bradford created an algorithm to help clinicians select appropriate pharmacologic interventions. Although it has not been validated, this algorithm provides a reasonable starting point.

In general, start treatment with an SSRI for low-risk individuals (Table 1, page 61). If this strategy is insufficient, consider augmentation with methylphenidate, naltrexone, or finasteride.

The next step would be to add oral MPA or CPA, 50 mg/d, which would partially inhibit testosterone and may allow some normal sexual functioning. Higher-dose oral MPA or CPA would be tried next. For higher-risk individuals or treatment failures, IM MPA or CPA would be offered next, followed by a GnRH agonist. For individuals at highest risk for re-offending, combinations of agents may be indicated.

This simple strategy is appealing, but in reality, treatment should be individualized. Choose medications based on the patient’s risk, wishes, and the previously mentioned clinical factors.

### References


---

**Table 4**

<table>
<thead>
<tr>
<th>Low-risk offenders</th>
<th>High-risk offenders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-referred</td>
<td>Offenses while receiving treatment</td>
</tr>
<tr>
<td>Open about offense</td>
<td>Minimization of offense</td>
</tr>
<tr>
<td>Situational offenders</td>
<td>Predatory offender</td>
</tr>
<tr>
<td>(ie, nonpredatory on known victim)</td>
<td>Violent offense</td>
</tr>
<tr>
<td>No hands-on offenses</td>
<td>Younger age</td>
</tr>
<tr>
<td>(ie, only child pornography, exhibitionism, voyeurism)</td>
<td>Social instability</td>
</tr>
<tr>
<td>No previous offenses</td>
<td>Paraphilic preference</td>
</tr>
<tr>
<td>Older age</td>
<td>(ie, preferential arousal to children or nonconsensual sex)</td>
</tr>
<tr>
<td>Social stability</td>
<td>Recurrent offenses</td>
</tr>
<tr>
<td>Nonparaphiliac preference (ie, preferential arousal to consensual sex with adults)</td>
<td>Psychopathy</td>
</tr>
<tr>
<td>Invested in treatment</td>
<td>Severe sexual sadism</td>
</tr>
<tr>
<td></td>
<td>Victim was a stranger</td>
</tr>
</tbody>
</table>

*Source: References 4,25,34*
Tailor treatment to the patient’s risk for recidivism and other clinical factors. Start with an SSRI for lower-risk patients. Consider oral or IM medroxyprogesterone or gonadotropin-releasing hormone agonists for those with higher risk.

Related Resources


Drug Brand Names

- Cyproterone acetate • Androcur
- Medroxyprogesterone acetate • Depo-Provera, Provera
- Finasteride • Propecia, Proscar
- Fluoxetine • Prozac
- Methylphenidate • Ritalin
- Fluvoxamine • Luvox
- Naltrexone • ReVia
- Paroxetine • Paxil
- Sertraline • Zoloft
- Gosarin • Zoladex
- Leuprolide • Eligard, Lupron
- Sertraline • Trileptal
- Triptorelin • Trelstar Depot

Disclosure

Dr. Booth reports no financial relationship with any company whose products were mentioned in the article or with manufacturers of competing products.

Bottom Line

Pharmacologic treatment of male sex offenders can decrease deviant sexual behavior. Tailor treatment to the patient’s risk for recidivism and other clinical factors. Start with an SSRI for lower-risk patients. Consider oral or IM medroxyprogesterone or gonadotropin-releasing hormone agonists for those with higher risk.