Benign Prostatic Hyperplasia: An Update and New Options for Treatment

Benign prostatic hyperplasia (BPH), or enlargement of the prostate gland, is common in men and almost universally associated with aging. This article gives an overview of BPH and reviews potential treatments including emerging options.

Hereditary angioedema: updated options for management and treatment

Hereditary angioedema (HAE) is a rare genetic disorder that is characterized by episodic subcutaneous and submucosal edema occurring in the extremities, abdomen, or rarely the larynx. This article looks at treatment options for this potentially deadly disorder.

Risk Evaluation and Mitigation Strategies (REMS) - Education Guide

The FDA Amendments Act of 2007 (FDAAA), effective March 25, 2008, implemented the Risk Evaluation and Mitigation Strategy (REMS), designed to ensure that drug benefits outweigh risks. The REMS program allows access to potentially serious risk medications, which otherwise may never have been approved. Approximately 180 medications, including generic and biologic products, currently fall under REMS review.

Edurant™: The Latest Non-Nucleoside Reverse Transcriptase Inhibitor for HIV

Rilpivirine (Edurant™), the fifth non-nucleoside reverse transcriptase inhibitor (NNRTI), was FDA approved in May 2011. Medications in this unique class bind to the enzyme reverse transcriptase, blocking RNA and DNA-dependent DNA polymerase activities including HIV-1 replication.¹

Benign Prostatic Hyperplasia: An Update and New Options for Treatment

Justinne Guyton, PharmD, Matt Hill, PharmD, Robert Wilson, PharmD and Debbie Minor, PharmD

Benign prostatic hyperplasia (BPH), or enlargement of the prostate gland, is common in men and almost universally associated with aging. Prevalence begins to increase exponentially beginning around age 40, and about half of men over age 75 have some symptoms of BPH.¹ The Massachusetts Male Aging Study associated higher free prostate specific antigen (PSA), heart disease, and the use of beta blockers with an increased risk of BPH.² Cigarette smoking (<1 pack/day) and higher levels of physical activity were associated with a decreased risk of BPH. Variation in sexual activity, alcohol intake, body mass index, diastolic blood pressure, diabetes and decreased serum androgen levels did not alter risk.² Race has some influence, but only in severity. Black men under 65 years may be more likely to require treatment for BPH than white men.¹

Though enlargement of the prostate gland typically begins in middle age, symptoms usually do not present for several years and may vary over time. Hypertrophy of the bladder detrusor muscle tends to initially compensate for the compression caused by prostate enlargement. As hyperplasia and
Compression progression, obstruction of the urethra occurs causing increased urinary flow resistance and impaired detrusor muscle response. This leads to lower urinary tract symptoms (LUTS) such as hesitancy, incomplete emptying, intermittency, post-void dribbling and decreased force of stream.

**Treatment of BPH**

Older age and the presence of functioning Leydig (i.e. testosterone producing) cells in the testes are essential for the development of BPH. It is currently thought that the connective stromal tissue of the prostate becomes increasingly sensitive to dihydrotestosterone, the active form of testosterone, over time, specifically in the periurethral zone. Men without BPH tend to show testosterone receptor expression primarily in the epithelial, fluid-producing tissue. In contrast, patients with BPH express this receptor in a more heterogeneous fashion, promoting an increase in volume over the entire gland. This is often referred to as the static component of BPH. Another factor contributing to BPH is the dynamic component, characterized by relatively high androgen tone in the prostatic smooth muscle mediated by the alpha adrenergic receptor. Stimulation of this receptor causes increased smooth muscle contraction and further decreases urethral lumen diameter.

The treatment for BPH varies based on the type and severity of symptoms and may be unnecessary in asymptomatic patients. In general, pharmacological treatment is often effective and attempted before considering invasive surgery. Patients with severe or long-standing symptoms may ultimately require surgical intervention.

The pharmacological treatment of BPH is primarily approached with three classes of medications: alpha\(_1\) adrenergic blockers (alpha blockers), 5-alpha reductase inhibitors (5-ARIs), and the newly approved phosphodiesterase type 5-inhibitor (PDE5-I). Patients may require a combination of these therapies, depending on symptoms and their severity. The static or volume component of BPH can be managed by using 5-ARIs such as finasteride and dutasteride. These medications improve symptoms over four to five months by reducing cell number and density in the prostate stroma, through inhibition of testosterone conversion to active dihydrotestosterone.

The dynamic component of BPH is approached using alpha blockers. Five are approved in the US for the treatment of BPH: terazosin, doxazosin, tamsulosin, alfuzosin, and silodosin. These are all long acting but differ in receptor specificity and potential adverse effects. By inhibiting the alpha receptor, these agents cause decreased smooth muscle contraction within the prostate. Three subtypes of the alpha receptor have been identified: alpha\(_{1A}\), alpha\(_{1B}\), and alpha\(_{1D}\). Alpha\(_{1B}\) and alpha\(_{1D}\) mediate vascular smooth muscle contraction while alpha\(_{1A}\) mediates urethra and periurethral smooth muscle contraction. The receptor selectivity of the alpha blockers varies between agents.

The American Urological Association (AUA) has traditionally recommended watchful waiting in patients with mild symptoms (AUA-Symptom Index score <8) and moderate or severe symptoms (AUA-Symptom Index score ≥8) secondary to BPH who are not bothered by their LUTS. Alpha blockers are recommended for the treatment of patients with bothersome moderate to severe LUTS. An update to the AUA guidelines added the option of combination therapy with an alpha\(_1\) blocker and 5-alpha reductase inhibitor for these patients.

Gonadotropin-releasing hormone (GnrH) agonists and antiandrogens are also used in the treatment of BPH, though the resulting androgen deficiency and sexual dysfunction makes these agents unacceptable for many patients.

Patients with severe symptoms of BPH may require prostatectomy performed either transurethrally or suprapubically. These patients may have problems with adherence or be unresponsive to drug therapy. Transurethral resection of the prostate (TURP) is also used and does not result in entire
prostate removal. In this procedure an endoscope is inserted into the urethra to remove the inside core of the prostate. Though relatively less invasive, symptoms may reoccur over time with this procedure as tissue regeneration occurs.\(^8\)

**A New Option for BPH - Phosphodiesterase-5 Inhibitors**

In The Multinational Survey of the Aging Male (MSAM-7), an increased incidence of sexual dysfunction was found in men with LUTS, especially in those older and with severe symptoms.\(^9\) Although epidemiologic evidence links BPH and erectile dysfunction (ED), the specific etiology has not been determined. In recent years, pharmacotherapy options that target symptoms of both have been evaluated, with positive evidence emerging for the PDE5-Is and one recent medication approval. This is reasonable as the phosphodiesterase isoenzyme 5 regulates smooth muscle tone in the prostate, penile corpus cavernosum, bladder and vasculature.

The effect of tadalafil (Cialis\(^\text{®}\)) was evaluated in three randomized, controlled trials of 12 weeks duration in approximately 2000 men with moderate to severe symptoms of BPH. Outcomes measured included patient perceived changes in symptoms as measured by the International Prostate Symptom Score (IPSS, baseline >7) and the change in maximum urinary flow rate. The International Index of Erectile Function-Erectile Function (IIEF-EF) questionnaire was used to evaluate reported symptoms of sexual dysfunction in men with ED. IPSS assesses both the irritative and obstructive symptoms of BPH using seven questions. Scores range from 0-35, with higher numbers representing an increased severity of symptoms. Scores for the IIEF-EF range from 1-30, with low scores representing increased sexual dysfunction. Results from the three trials are summarized in the table below. The mean urinary flow rate increased from baseline in each of these studies, though it was not statistically significant when compared to placebo.\(^10\)-\(^12\)

<table>
<thead>
<tr>
<th><strong>Table: Change in Score Over 12 Weeks</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trial</strong></td>
</tr>
<tr>
<td>Roehrborn et al.(^{10}) (n=1058)</td>
</tr>
<tr>
<td>Porst, et al.(^{11}) (n=325)</td>
</tr>
<tr>
<td>Egerdie et al.(^{12}) (n=606)</td>
</tr>
</tbody>
</table>

* 55% of study patients who were sexually active with ED

Subsequent to the findings of these studies submitted for FDA review, tadalafil was approved in September 2011 for daily use in patients with BPH or BPH with ED. The recommended dose is 5 mg daily, similar to the daily dose for ED (2.5 or 5 mg), but lower than the as needed dose (5, 10 or 20 mg). As other medication classes used for BPH can potentially cause sexual dysfunction, use of PDE5-I may provide another treatment option for men who have sexual side effects related to these medications.\(^13\) Further studies are needed to more adequately define both the benefits and risks of combination therapy. Tadalafil is not currently recommended in combination with alpha blockers for the treatment of BPH. Caution is advised when using the combination for treatment of ED.\(^13\)

Patients should be advised to take tadalafil at the same time each day, without regard to timing of sexual activity. As with prn use, daily use of tadalafil can potentiate the hypotensive effects of nitrates, alpha blockers, antihypertensives and alcohol. Concurrent use with potent CYP 3A4 inhibitors or inducers may increase or decrease tadalafil exposure. If a patient is already receiving an alpha blocker, prescribing guidelines recommend the discontinuation of the alpha blocker at least 1 day prior to the initiation of tadalafil for BPH.\(^13\)
Conclusion

Pharmacotherapy options for BPH have advanced over the last ten to fifteen years, allowing many patients to achieve symptom improvement and an increased overall quality of life. While there are caveats to the selection and use of each of the primary classes of medications indicated for BPH, there is insufficient evidence at this time to suggest one agent or class as clinically superior to another. The increased recognition of the concurrent occurrence of ED and BPH allows consideration for a common treatment regimen for many men. Several studies establish the significant improvement in BPH symptoms with and without ED, leading to this new use for PDE5-Is and the expanded indication for tadalafil.

References

Hereditary angioedema (HAE) is a rare genetic disorder that is characterized by episodic subcutaneous and submucosal edema occurring in the extremities, abdomen, or rarely the larynx.\textsuperscript{1,2} It is estimated to affect 1 in 50,000 people and is thought to be caused by a disruption of C1 esterase inhibitor activity. Patients with HAE may have low plasma levels of C1 inhibitor (type 1) or produce inactive protein despite normal levels (type 2). The C1 esterase inhibitor controls activation of the systemic complement, coagulation, and contact cascades.\textsuperscript{2} Diminished inhibitor activity leads to largely unopposed bradykinin. HAE attacks then follow as bradykinin stimulates vasodilation, increases vascular permeability, causing edema and can even cause bronchoconstriction.\textsuperscript{3}

A person may be born with the protein deficiency and HAE or develop it later in life. Approximately one in four patients “acquire” this condition from spontaneous gene mutations.\textsuperscript{4} Most patients experience their first symptoms of HAE before the age of 20. Symptoms typically progress over 8-24 hours and resolve without treatment after 48-96 hours. Patients generally experience periods of remission that last less than 1 year. Skin swelling most often occurs in the face and extremities. Some cases are minor and do not require treatment, while others are extremely painful and may cause immobility and decrease quality of life. Gastrointestinal edema tends to be severe with nonspecific symptoms such as abdominal pain, cramping, vomiting, diarrhea, and nausea. The most common cause of death associated with HAE occurs from swelling of the larynx. Fortunately, this is uncommon, occurring in less than 1% of attacks. Laryngeal edema, when it happens, generally begins with symptoms of dysphagia, hoarseness, and dyspnea and progresses over 8-12 hours.\textsuperscript{1,5}

HAE differs from angioedema caused by hypersensitivity reactions in that it does not produce urticaria or pruritus or respond completely to antihistamines or epinephrine.\textsuperscript{3} Treatment for acute attacks of HAE includes therapies that decrease bradykinin production, block bradykinin receptors, or increase the amount of C1 esterase inhibitor. Some patients require prophylaxis of HAE attacks on a short-term basis before surgical and dental procedures; however, patients with severe laryngeal involvement or those experiencing frequent attacks may require long-term prophylactic treatment. New options for both treatment and prophylaxis of HAE have recently become available in the United States.

Treatment of HAE

Treatment options for acute attacks of HAE include fresh frozen plasma (FFP), C1 inhibitor concentrate, ecallantide, or icatibant. Androgens (danazol / stanozolol), antifibrinolytics (tranexamic acid / aminocaproic acid), FFP (fresh frozen plasma), or C1 inhibitor concentrate are used for prophylaxis.\textsuperscript{1,3} These agents and dosing information are highlighted in the Table below. Prior to the availability of newer options, FFP was the only therapy for acute attacks. No longer recommended by the international guidelines, FFP includes protein precursors to bradykinin which could theoretically worsen attacks.\textsuperscript{5} In 2007, a review reported that FFP was not associated with increased or worsening attacks; however, its efficacy has still not been established in clinical trials.\textsuperscript{1}

Plasma-derived C1 inhibitor (pdC1INH) has been considered first-line therapy for HAE exacerbations for many years outside the United States. Transmission of viral infections through these products has been of concern, though extensive screening and purification now make this unlikely.\textsuperscript{1} Berinert®, a pasteurized form of human C1 inhibitor, was approved for treatment of HAE attacks in the United States in 2009.\textsuperscript{1} In clinical trials, patients had a median time to symptom relief of 48 minutes with Berinert® versus more than 4 hours with placebo.\textsuperscript{6} Cinryze® is a nanofiltered preparation of pdC1INH
that is approved for prophylaxis of HAE exacerbations. In clinical trials, Cinryze® decreased the average attack severity and reduced the duration by 66% in days of swelling. Both Berinert® and Cinryze® may be self-administered after patients receive proper education from their healthcare provider. Prescribing information for Berinert® recommends that patients seek medical attention after self-administration for treatment of a laryngeal attack. A recombinant form of C1INH, developed to circumvent the concerns with plasma-derived products, is currently approved in Europe and in phase III trials in the United States.

Ecallantide (Kalbitor®), a kallikrein inhibitor, was FDA approved in 2009 for the treatment of acute HAE attacks. Inhibition of kallikrein, a protein precursor to bradykinin, should lead to decreased bradykinin levels and activity during an attack. Because ecallantide is not derived from human plasma products, there is no concern of viral transmission. Ecallantide must be given by a healthcare professional so the manufacturers have instituted a home infusion service for patient convenience. Nurses are available 24 hours per day for administration of the medication. Prescribing information for ecallantide includes a Black Box Warning for anaphylaxis. In EDEMA-3 and EDEMA-4, the two clinical trials used to gain FDA approval, patients treated with ecallantide had significantly greater decreases in symptom scores at 24 hours versus placebo; however, scores were not significantly different 4 hours after treatment initiation.

Icatibant (Firazyr®), a competitive bradykinin B₂ receptor inhibitor, is the most recently FDA-approved medication for the treatment of acute HAE attacks. The medication is designed for self-administration, after proper instruction from a healthcare professional. In clinical trials, the median time to 50% symptom reduction ranged from 2 to 2.5 hours with Firazyr®, compared to 4.6 hours for placebo in the FAST-1 trial and 19.8 hours in the FAST-3 trial. In the active-controlled FAST-2 trial, patients treated with tranexamic acid had 50% symptom reduction in 12 hours versus only 2 hours in those treated with Firazyr®. It should be noted, however, that tranexamic acid is not considered a first-line agent for acute attacks, because its onset of action for HAE takes several days. Nearly all patients who received icatibant in clinical trials reported injection site pain (97%).

Other options for prophylaxis of HAE attacks include androgens and antifibrinolytics. Synthetic anabolic androgens are used to increase C1INH plasma levels, although the mechanism behind this activity is not fully understood. Danazol and stanozolol are considered the drugs of choice for this indication. Dosing for both should be titrated to the lowest dose that still confers benefit. Because of the virulizing effects of these medications, they should not be used in pregnant women or in children. Antifibrinolytics such as aminocaproic acid and tranexamic acid (not available in the United States) are the preferred agents in children and pregnant women. Their mechanism of action in controlling HAE attacks is also unknown.

For some patients with HAE, short-term prophylaxis for surgical or dental procedures is important to prevent a potential attack. High doses of androgens are generally used; however, they must be started 5-7 days before the scheduled procedure. Alternatively, FFP may be infused several hours prior to the procedure. While newer treatments are not indicated for this, there have been several case reports and smaller trials indicating that pdC1INH may be a viable option for short-term prophylaxis of attacks in the future.

Conclusion
HAE is a chronic and complex genetic disease that requires specialized care and a multidisciplinary approach for treatment. In the past, treatment options available for acute attacks have been limited. Several therapies have emerged now that may make HAE more manageable and offer options for initial self-management of acute attacks.

<table>
<thead>
<tr>
<th>Product</th>
<th>Use</th>
<th>Dosing Recommendation</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berinert® (pdC1INH)</td>
<td>Acute</td>
<td>20 units per kilogram; slow IV, ~4 ml/min</td>
<td>May be self-administered</td>
</tr>
<tr>
<td>Cinryze® (pdC1INH)</td>
<td>Prophylaxis – Long-term</td>
<td>1000 units twice weekly, IV over 10 min</td>
<td>May be self-administered</td>
</tr>
<tr>
<td>Kalbitor® (ecellantide)</td>
<td>Acute</td>
<td>30 mg SC given as 3 separate injections of 10 mg (1 ml) each</td>
<td>Must be given by a healthcare professional, at 1st sign of attack</td>
</tr>
<tr>
<td>Firazyr® (icatibant)</td>
<td>Acute</td>
<td>30 mg SC (abdomen)</td>
<td>May be self-administered. Can repeat dose twice at 6 hr intervals if needed</td>
</tr>
<tr>
<td>Danazol</td>
<td>Prophylaxis – Short and long-term</td>
<td>200 mg daily or every other day PO for long-term prophylaxis 200 mg TID PO 5-7 days prior to procedure for short-term</td>
<td>Contraindicated in pregnancy and children. Use lowest dose possible.</td>
</tr>
<tr>
<td>Stanozolol</td>
<td>Prophylaxis – Short and long-term</td>
<td>2 mg daily or every other day for long-term 2 mg TID PO 5-7 days prior to procedure</td>
<td>Contraindicated in pregnancy and children. Use lowest dose possible.</td>
</tr>
<tr>
<td>Amicar® (aminocaproic acid)</td>
<td>Prophylaxis – Long-term</td>
<td>1 gram PO 3-4 times daily</td>
<td>Less reliable than androgens in preventing attacks</td>
</tr>
</tbody>
</table>
References


Risk Evaluation and Mitigation Strategies (REMS) - Education Guide

Livia Macedo, Pharm.D., Deborah Minor, Pharm.D., Michael Todaro, Pharm.D., Sharon Dickey, Pharm.D., Kenneth Butler, PhD

The FDA Amendments Act of 2007 (FDAAA), effective March 25, 2008, implemented the Risk Evaluation and Mitigation Strategy (REMS), designed to ensure that drug benefits outweigh risks. The REMS program allows access to potentially serious risk medications, which otherwise may never have been approved. Approximately 180 medications, including generic and biologic products, currently fall under REMS review. Providers can play a vital role in REMS through following guidelines, patient counseling, monitoring efforts, and advocating for changes to improve the program. REMS requirements differ depending on risk of the drug and may include some or all of the following elements:

**Medication Guides**

The FDA may require a Medication Guide under the following circumstances:

- The drug product is one for which patient labeling could help prevent serious adverse effects.
- The drug product is one that has serious risks (relative to benefits) about which patients should be made aware because the information concerning the risks could affect the patient’s decision to use, or continue to use, the product.
- The drug product is important to health and patient adherence to directions for use is crucial to effectiveness.
A Medication Guide should be distributed in each of the following situations:

<table>
<thead>
<tr>
<th>Setting</th>
<th>Patient or Their Agent Requests</th>
<th>Each Time Drug Dispensed</th>
<th>With First Dispensing</th>
<th>Medication Guide is Materially Changed</th>
<th>Drug Requires ETASU with Specific Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient (e.g. hospital, nursing home)</td>
<td>R</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>R</td>
</tr>
<tr>
<td>Outpatient when dispensed to health care professional for administration to patient (e.g. clinic, dialysis, infusion center)</td>
<td>R</td>
<td>NR</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<tr>
<td>Outpatient when dispensed directly to patient or caregiver (e.g. retail pharmacy, hospital ambulatory pharmacy)</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
</tbody>
</table>

R=required; NR=not required

A Medication Guide should also be dispensed with every sample. Common medications requiring a Medication Guide include: pioglitazone (Actos), levofloxacin (Levaquin), varenicline (Chantix), bupropion (Wellbutrin XL), and oxycodone solution, among others.

**Communication Plans**
These are FDA-approved tools to support REMS implementation and inform providers about serious risks of drugs and safety protocols. Information may be disseminated by “Dear Health Care Provider” letters or through professional organizations. Medications requiring a communication plan include: liraglutide (Victoza), quinine sulfate, prasugrel (Effient), ticagrelor (Brilinta), and salmeterol (Serevent Diskus), among others.

**Elements to Assure Safe Use (ETASU)**
ETASU may be required to ensure safe access to medications that would otherwise be unavailable due to serious risks. Elements required may include enrollment in registry programs, focused training or certification, drug administration in limited settings (e.g. hospitals), documentation of safe use conditions, or specific patient monitoring. Examples of medications requiring ETASU include: rosiglitazone (Avandia), epoetin alfa (epogen/Procrit), oxycodone controlled-release tablets (Oxycontin), dofetilide (Tikosyn), and fentanyl sublingual (Abstral), among others.

**References and Additional Information**
Edurant™: The Latest Non-Nucleoside Reverse Transcriptase Inhibitor for HIV

Lucy Cadwallader

Rilpivirine (Edurant™), the fifth non-nucleoside reverse transcriptase inhibitor (NNRTI), was FDA approved in May 2011. Medications in this unique class bind to the enzyme reverse transcriptase, blocking RNA and DNA-dependent DNA polymerase activities including HIV-1 replication.¹

Rilpivirine is indicated in combination with other antiretroviral agents for the management of treatment naïve HIV infected adults. It is available as a single agent and in combination with the nucleoside reverse transcriptase inhibitors (NRTI) emtricitabine and tenofovir as the product Complera™. The Department of Health and Human Services recommends that the initial management of HIV treatment naïve patients consist of two NRTIs and either an NNRTI, a boosted protease inhibitor (PI), or an integrase strand transfer inhibitor (INSTI).¹,²

All NNRTIs may cause hepatotoxic reactions, including transaminase elevations, and may cause a rash.¹,³ Like several of the NNRTIs, rilpivirine is metabolized by CYP3A4 and is contraindicated with medications that can decrease its concentration due to CYP induction or increased gastric pH: carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, proton pump inhibitors, systemic dexamethasone, and St. John’s wort. Rilpivirine should be taken with food to increase absorption. The package information warns about the possibility of developing depressive disorders, fat redistribution, and immune reconstitution syndrome when starting therapy.¹

In clinical trials, rilpivirine was determined to be noninferior to the commonly used NNRTI efavirenz (Sustiva®). Product labeling warns that in pre-marketing trials, more patients with initial HIV-1 RNA loads > 100,000 copies/mL experienced virologic failure on rilpivirine compared to those with initial HIV-1 RNA loads < 100,000 copies/mL. In addition, the emergence of treatment resistance and cross-resistance to the NNRTI class was greater in the rilpivirine arm versus the efavirenz treatment arm.¹

A potential benefit of rilpivirine may be for use in pregnant women. Rilpivirine carries a pregnancy category B safety rating in contrast to efavirenz, which has human fetal risk and is classified as
pregnancy category D. All HIV-infected mothers should avoid breastfeeding due to the potential for HIV transmission. A brief comparison of the available NNRTIs is included below.

**Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs):**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosing</th>
<th>Comments / Warnings / Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delavirdine (Rescriptor®)</td>
<td>400 mg TID</td>
<td>Separate dose from antacid by 1 hour</td>
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<tr>
<td></td>
<td></td>
<td>Strong inhibitor of 2C9, 2C19, 2D6, 3A4</td>
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<tr>
<td></td>
<td></td>
<td>Pregnancy category C</td>
</tr>
<tr>
<td>Efavirenz (Sustiva®)*</td>
<td>600 mg daily</td>
<td>Take on empty stomach</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inhibits 2CP and 3A4 (moderate); induces 3A4 (strong)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pregnancy Category D</td>
</tr>
<tr>
<td>Etravirine (Intelence®)</td>
<td>200 mg BID</td>
<td>Take after full meal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pregnancy Category B</td>
</tr>
<tr>
<td>Nevirapine (Viramune®)</td>
<td>200 mg daily X 14 days; then 200 mg BID</td>
<td>BBW: Severe hepatotoxic reactions (risk &gt; first 6 weeks); life-threatening skin reactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3A4 inducer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pregnancy Category B</td>
</tr>
<tr>
<td>Rilpivirine (Edurant™)*</td>
<td>25 mg daily</td>
<td>Take with food</td>
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<tr>
<td></td>
<td></td>
<td>Do not use with drugs that increase gastric pH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3A4 metabolism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pregnancy Category B</td>
</tr>
</tbody>
</table>

*Available in combination. All are available for oral dosing.

References:


