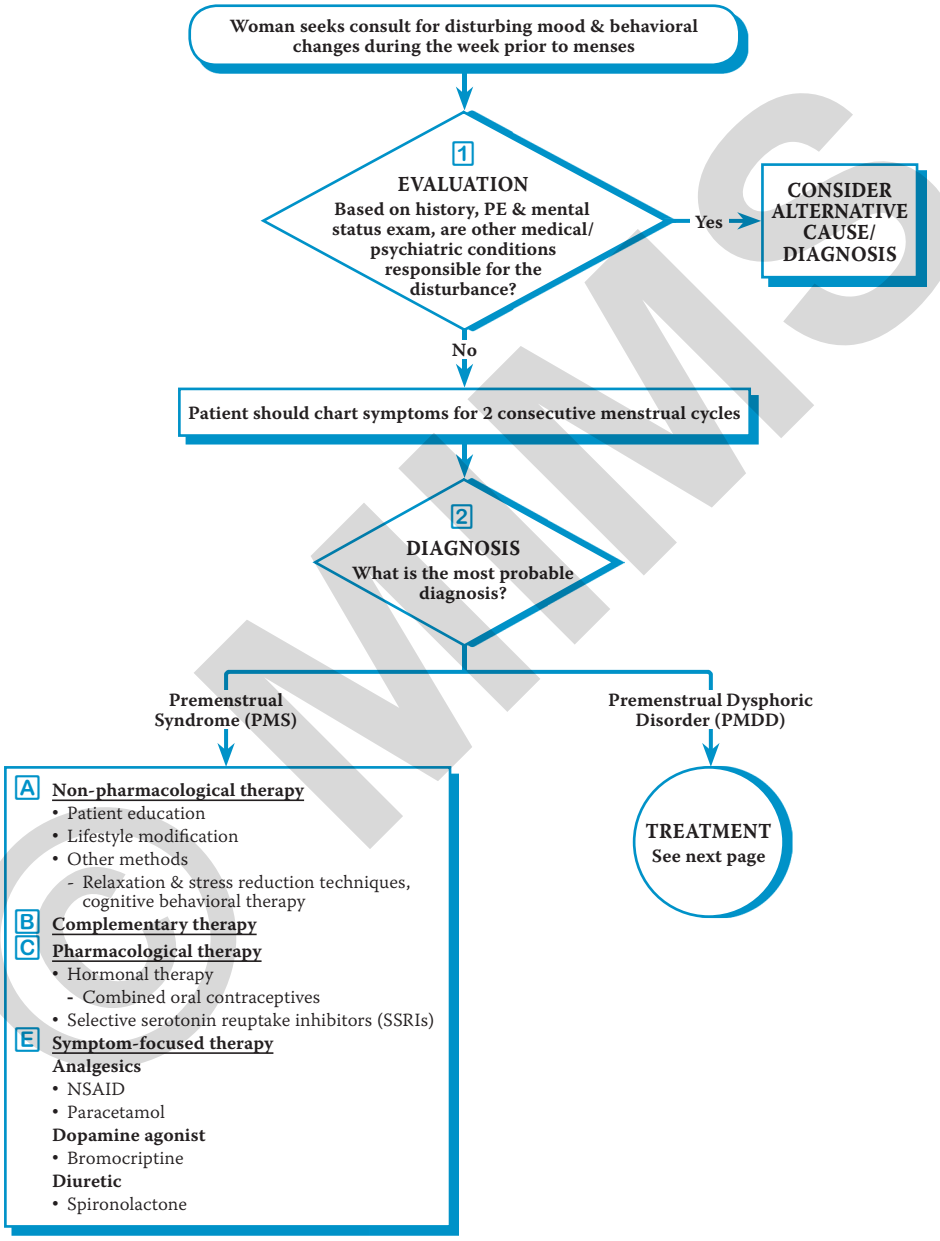
Premenstrual Dysphoric Disorder (1 of 13)



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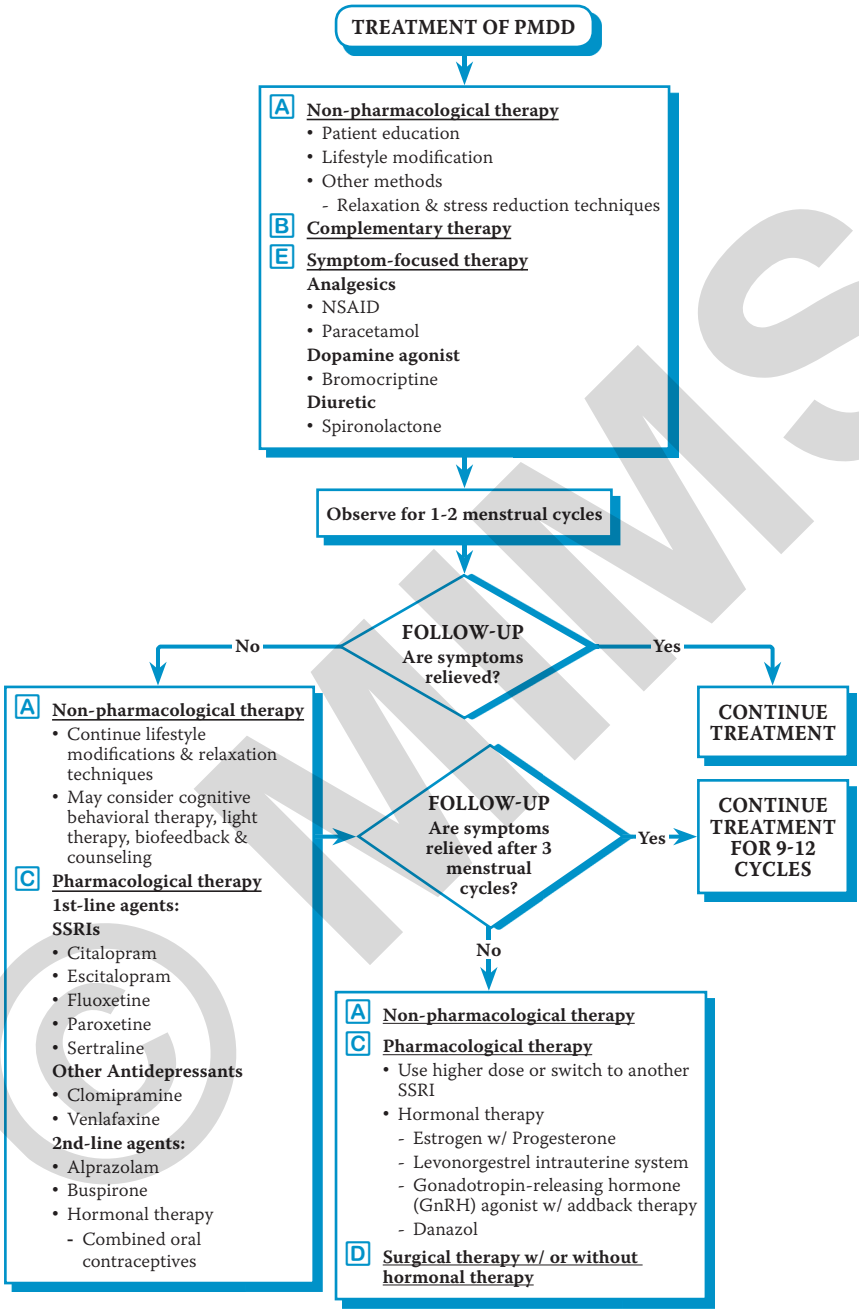

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1 EVALUATION

Underlying Medical & Psychiatric Disorders

The following medical conditions may mimic PMDD w/ premenstrual exacerbation:

- Allergies
- Anemia
- Asthma
- Autoimmune or collagen vascular disorders
- Chronic fatigue syndrome
- Endometriosis
- Endocrine disorders (DM, hypothyroidism)
- Epilepsy
- Hyperprolactinemia
- Irritable bowel syndrome
- Migraine
- Panhypopituitarism
- Polycystic ovarian disease

The following psychiatric conditions may mimic PMDD w/ premenstrual exacerbation:

- Anxiety disorders
- Bipolar disorder
- Bulimia
- Cyclothymic disorder
- Depression
- Dysthymic disorder
- Posttraumatic stress disorder
- Psychosocial (current victim of physical abuse or history of sexual abuse)
- Panic disorder

2 DIAGNOSIS

Premenstrual Syndrome (PMS)

- PMS is a group of recurrent mild to moderate physical &/or emotional symptoms occurring during the late luteal phase of the ovulatory cycle that do not usually interfere w/ the patient's usual level of function
  - Occurs in approximately 75% of women of reproductive age, among whom 20-50% report moderate to severe symptoms

Premenstrual Dysphoric Disorder (PMDD)

- PMDD is a cyclical disorder presenting w/ distressing mood & behavioral symptoms that occur during the late luteal phase of the ovulatory cycle; it is a severe form of PMS
- PMDD results in considerable impairment of the patient's personal functioning
  - Occurs in approximately 5% of women of reproductive age

Diagnostic Criteria for PMDD

- Presence of ≥1 of the 1st four symptoms & ≥5 of any symptom occurring during the last week of the luteal phase w/ remission starting within a few days after the onset of menses & absent in the week postmenses
  1. Appreciable depressed mood, feeling of hopelessness or self-depreciation
  2. Marked tension, anxiety or feelings "on edge" or "keyed up"
  3. Appreciable affective lability such as sudden sadness or tearfulness or having increased sensitivity to rejection
  4. Continual & marked anger or irritability or increased interpersonal conflicts
  5. Decreased interest in usual activities
  6. Subjective feeling of difficulty in concentrating
  7. Lethargy, marked lack of energy, easy fatigability
  8. Hypersomnia or insomnia
  9. Subjective feeling of being overwhelmed or out of control
  10. Change in appetite, overeating or cravings for certain foods
  11. Physical symptoms (eg breast swelling/tenderness, sensation of bloating/weight gain, joint or muscle pain, headache)
- Appreciable interference w/ school/work or w/ usual social activities or relationships w/ others
- The disturbance is not a mere exacerbation of the symptoms of another disorder (eg major depression, panic disorder)
- Confirmation of the 3 criteria above by prospective daily ratings during at least 2 consecutive symptomatic menstrual cycles
  - Diagnosis may be provisional prior to confirmation by daily ratings
- The symptoms are not due to the effects of a medication or another medical condition, other treatment, or drug of abuse

Diagnosis & Treatment Strategies

- Take a thorough medical history
  - Personal & social history may reveal trauma or sexual abuse
- Patient should record symptoms for 2 menstrual cycles during which lifestyle-related interventions are begun
  - May use standardized daily symptom calendars such as the Calendar of Premenstrual Experiences (COPE) or the Daily Record of Severity of Problems
    - COPE, developed by the University of California, San Diego (UCSD), is a daily scoring sheet that assigns a severity score to the common physical (eg bloating, swelling, headache, breast tenderness) & behavioral symptoms (eg depression, irritability, confusion, angry outbursts) during the menstrual cycle
    - A score of <40 during days 3-9 of the menstrual cycle added w/ score of >42 during the last 7 days of the cycle has been demonstrated to be a predictor of women meeting inclusion criteria for PMDD
  - If patient remains symptomatic after 2 months of charting & lifestyle modifications, then pharmacotherapy should be considered
  - If patient w/ PMS fails pharmacotherapy & has severe symptoms, management by a multidisciplinary team utilizing a holistic approach (eg gynecologist, mental health practitioner, dietitian) may be warranted
- A one-time screening process using a checklist of common symptoms may be more feasible in clinical practice

A NON-PHARMACOLOGICAL THERAPY

Goals of Therapy
- Reduce symptoms
- Improve social & occupational performance needed for improved quality of life

Patient Education
- Emphasize the need to seek help due to the following reasons:
  - PMDD tends to recur each cycle & may become severe over time
  - This dysfunction can be readily diagnosed & effectively treated
- Advise regarding the benefits & risks of each therapeutic agent & how to safely stop drug intake
- Inform the patient regarding the mixed results of studies on complementary medicines
- Educate both the patient & the family/spouse as this disorder impacts on the entire family context

Lifestyle Modification

Diet Modification
- Dietary changes can have a noticeable impact on PMS severity
  - Reduction of caffeine intake may diminish anxiety & irritability
  - Decreasing Na intake can lessen bloating & edema
  - Patients should also be encouraged to reduce intake of refined sugar & eat small balanced meals rich in complex carbohydrates

Increase in Physical Exercise
- Has been shown to significantly improve mood & decrease lethargy
- Evidence of effect is largely anecdotal but can be advised as part of healthy lifestyle
- Aerobic exercise for 20-30 minutes, 3-4x/week has been recommended
- Reduction of body weight to within 20% of ideal is an appropriate goal

Other Methods
- In conjunction w/ pharmacological therapy, the following techniques may offer significant improvement in premenstrual symptoms:
  - Relaxation & stress reduction, cognitive behavioral therapy, light therapy, yoga, guided imagery, reflexology, massage therapy, biofeedback, acupuncture, counseling
    - A study showed long-term efficacy of cognitive behavioral therapy for premenstrual disorders
- Adopting a regular sleep-wake pattern may alleviate distress & discomfort associated w/ sleep irregularities
- Avoiding stressful activities during the premenstrual period may be helpful

B COMPLEMENTARY THERAPY

Dietary Supplements

Calcium
- Clinical trial showed that 1200 mg of $CaCO_3$ per day can offer significant reduction in symptoms such as pain & food cravings as well as improvement of negative affect
- Supplementation w/ calcium & vitamin D may relieve symptoms of PMS or PMDD

Magnesium, Tryptophan, Vitamin E
- Limited data shows some benefits of using these supplements in women w/ PMDD

Vitamin B_6
- Clinical studies have shown that daily doses of 50-100 mg of vitamin B_6 can reduce severity of premenstrual depressive & physical symptoms of PMS & PMDD
- Caution patient on the risk of developing peripheral neuropathy at high doses (≥200 mg/day)

Herbal Therapy
- Herbal therapies have been tried on women w/ PMS & may have some positive effects

Chaste Tree Berry
- Chaste tree berry (*Vitex agnus castus*) may reduce prolactin levels & offer relief for breast engorgement, irritability, anger, mood swings & headache
  - Has a dopaminergic effect & indirect anti-prolactin effect
- May have efficacy similar to that of the antidepressant Fluoxetine

Evening Primrose Oil
- Has been shown by some studies to have some benefit in women w/ PMS & those w/ cyclical breast symptoms

Ginkgo Biloba
- A placebo-controlled randomized controlled trial showed significant reduction in the physical & psychological effects in women w/ PMS in the first cycle of treatment

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C PHARMACOLOGICAL THERAPY

Selective Serotonin Reuptake Inhibitors (SSRIs)

- Considered the 1st-line treatment for severe PMDD
- Selective blockers of the reuptake of serotonin at presynaptic neurons w/ little, if any, effect on muscarinic, histaminergic, adrenergic or serotonergic receptors
- Treatment regimen can be given continuously throughout the menstrual cycle, during the luteal phase or at the start of symptoms & choice would depend on patient preference, predictability of symptom manifestation or physician evaluation that symptoms are present & worsen during the premenstrual phase
  - Timing of treatment during the luteal phase & that wherein dosing is done for the whole cycle are both effective
  - If given continuously, SSRIs should be stopped gradually to prevent withdrawal symptoms
- Potential adverse effects w/ treatment include decreased libido, fatigue, insomnia, nausea, & somnolence, though these can be reduced w/ use of luteal-phase regimens
- As PMS symptoms will subside during pregnancy, SSRI therapy should be stopped before & during pregnancy due to possible congenital malformations

Fluoxetine

- Clinical studies have shown that Fluoxetine is superior to placebo in decreasing both emotional & physical symptoms of PMDD
  - Shown to have significant rate of response during the 1st treatment cycle
  - Efficacy of Fluoxetine is the same whether used only during the luteal phase (intermittent dosing) or throughout the full menstrual cycle (continuous dosing)
- The use of Fluoxetine in PMDD is approved by the USFDA

Sertraline

- Sertraline has shown similar efficacy to Fluoxetine
- Clinical studies have shown improvement in both emotional & physical symptoms
  - Improvement in symptoms has been noted within the 1st cycle
  - A significantly effective treatment using intermittent or continuous dosing
- The use of Sertraline in PMDD is approved by the USFDA

Other SSRIs that have shown efficacy

- Citalopram & Paroxetine have demonstrated efficacy in PMS & PMDD clinical trials
  - One study w/ Citalopram showed that intermittent dosing may be preferred over continuous treatment, though both were superior to placebo therapy
  - Citalopram has been used in doses of 10-30 mg/day continuously or intermittently during the luteal phase
  - Paroxetine has been used in doses of 10-30 mg/day continuously or intermittently during the luteal phase
    - Risk for congenital abnormalities is increased when taken during the 1st trimester of pregnancy
- Fluvoxamine has shown mixed results in treatment of PMDD
- Escitalopram appears to demonstrate similar efficacy as that of Citalopram

Other Antidepressants

Clomipramine

- Serotonergic tricyclic antidepressant
- Shown to be more effective than placebo in the treatment of PMDD using either continuous or intermittent dosing

Venlafaxine

- Serotonin & noradrenaline reuptake inhibitor
- Daily dosing of immediate-release Venlafaxine was reported to be superior to placebo in reducing emotional & physical symptoms of PMDD

Anxiolytics

Alprazolam

- Alprazolam is an intermediate-acting benzodiazepine considered 2nd-line in PMDD treatment
- Results of clinical studies were mixed & use is restricted by risk of dependence & withdrawal
- Use should be limited to luteal-phase dosing
  - One study found no withdrawal symptoms when intermittent luteal-phase dosing was used

Buspirone

- A serotonergic agonist that appears to have weak beneficial effects on premenstrual symptoms
- Decreases irritability symptoms in women w/ PMDD

C PHARMACOLOGICAL THERAPY (CONT'D)

Hormonal Therapy
- Hormonal intervention is considered if treatment w/ other methods was unsuccessful
- Symptoms of PMDD may resolve if ovulation is suppressed, inducing anovulation & amenorrhea
- Use is limited by occurrence of menopausal symptoms such as hot flushes, vaginal dryness, fatigue, irritability, cardiac problems & osteopenia
  - Addback therapy w/ Estradiol & Progestogen is used to avoid above side effects but may cause premenstrual disorder-like symptoms

Oral Contraceptives (OCs)
- May be considered 2nd-line therapy in patients unresponsive to SSRIs
- Women, whose priority is contraception, prefer an OC rather than an SSRI as 1st-line treatment
  - If OC monotherapy provides inadequate relief of symptoms, an SSRI may be added
- Drospirenone/Ethinyl estradiol in a 24/4 regimen improved mood & physical symptoms in patients w/ PMDD
- Patients w/ PMS may be effectively treated w/ Drospirenone-containing combined oral contraceptives
- Continuous rather than cyclical use of contraceptive pill is suggested by current data in those w/ PMS

Estrogen
- Relatively straightforward & effective therapy
- Transdermal Estrogen (gel or patch) or SC implants are recommended over oral therapy
- Progestogen is necessary unless the patient has had a hysterectomy
  - Prevents irregular bleeding & endometrial hyperplasia (oral or vaginal progesterone at a cyclical 10-12 day treatment course)
  - Combination of percutaneous Estradiol & cyclical progestogen has been effective in managing severe PMS
  - Use lowest possible dose to reduce adverse effects of progestogen when transdermal Estrogen is used
  - Investigate immediately any unscheduled bleeding in patients on short courses of progestogen treatment or those receiving low doses
  - Micronized progesterone is preferred over progestogen for progestogenic opposition as it has less potential for causing PMS-like symptoms
- Levonorgestrel intrauterine system (LNG-IUS) protects against endometrial hyperplasia
  - When ovulation is suppressed w/ Estradiol, use intrauterine methods of contraception
  - Low levels of Levonorgestrel can initially cause PMS-type adverse effects & bleeding
- Treatment w/ opposed Estradiol therapy should be individualized w/ the benefits & risks of therapy considered

Progesterone/Progestogens
- Limited benefit has been shown in efficacy studies done w/ progesterone or progestogens in the treatment of PMS

Gonadotropin-releasing Hormone (GnRH) Agonists
- Act on the hypothalamus to decrease FSH & LH secretion resulting in anovulation & decreased estrogen & progesterone synthesis
- May be given to patients for 3 months to aid in the diagnosis of PMS if charted symptoms are inconclusive
- Highly effective & should be given to patients w/ severe PMS symptoms that do not respond to other treatment options
- Have been shown to be superior to placebo in alleviation of PMS complaints such as irritability & depression along w/ physical symptoms
- Cause typical menopausal symptoms (eg flushing, osteoporosis) so treatment should be limited to 6 months
  - If to be given for >6 months in patients w/ severe PMS, addback therapy should be utilized, eg Tibolone or continuous combined hormone replacement therapy
  - Stop treatment if there is a significant decline in bone density from annual BMD measurements

Danazol
- Efficacy in reducing PMDD symptoms is linked to induction of anovulation
  - Low-dose administration during the luteal phase helps w/ mastalgia
- Use is limited by occurrence of side effects (eg amenorrhea, weight gain, acne, facial hair & nausea)
  - Long-term use leads to masculinization; hence, Danazol is currently rarely used but if it is, it must be given in low doses
  - Advise patient regarding contraception use due to possible virilization of the female fetus

D SURGICAL THERAPY

- Considered only as a last resort when more conservative treatments have failed
- Conduct a preoperative trial of GnRH agonist therapy to assess benefit & to ensure tolerance to hormonal therapy
- Patients <45 years old should be counseled to use hormonal therapy after surgery
- Ovary-sparing endometrial ablation & hysterectomy in women w/ severe PMS are not recommended

Hysterectomy w/ Bilateral Salpingo-oophorectomy

- May be considered if patient failed medical therapy, requires long-term GnRH agonist therapy, or has other gynecological conditions warranting surgery
- Has been demonstrated to exert beneficial effect on mood & physical symptoms
- Long-term Estrogen therapy must be given to prevent Estrogen deficiency symptoms

Bilateral Oophorectomy

- Permanent invasive method which effectively abolishes symptoms
  - Progestogen requirement w/ any subsequent hormonal therapy regimen after surgery may again cause PMS-like symptoms

E SYMPTOM-FOCUSED THERAPY

Analgesics

- Effective treatment for dysmenorrhea
- Ibuprofen, at doses of up to 1,000 mg/day, can reduce breast pain, headaches, back pain

Dopamine Agonist

- Bromocriptine may offer relief to women w/ cyclic mastalgia

Diuretic (Spironolactone)

- Spironolactone has antimineralocorticoid & antiandrogenic properties
  - When dosed at 100 mg/day, was shown by a study to be more effective than placebo in reducing irritability, depression, somatic symptoms, craving for sweets, & breast tenderness
  - May also improve premenstrual bloating & weight gain
  - Recommended to be given only during the luteal phase

Dosage Guidelines

ANXIOLYTICS

Drug	Dosage	Remarks
Alprazolam	0.375-1.5 mg PO 24 hrly during the luteal phase	**Adverse Reactions** • Dependence & withdrawal symptoms can occur especially in patients w/ history of drug dependence • CNS effects (sedation, drowsiness, muscle weakness, ataxia; less commonly slurred speech, vertigo, headache, confusion; paradoxical excitement may occur) **Special Instructions** • Intermittent use during luteal phase may reduce the risk of drug dependence
Buspirone	20-30 mg/day PO divided 8-12 hrly	**Adverse Reactions** • CNS effects (dizziness, headache, nervousness, lightheadedness, excitement, paresthesia, sleep disturbances, tremor, incoordination); ENT effects (tinnitus, nasal congestion, sore throat); Other effects (nausea, chest pain, rash) • Less sedation & lower potential for dependence compared to other anxiolytics **Special Instructions** • Use w/ caution in patients w/ renal or hepatic dysfunction or seizure disorder • Withdraw the drug gradually in patients taking benzodiazepines • May impair ability to drive or operate machinery

COMBINATION ORAL CONTRACEPTIVES (COCs)

Drug	Progestin (mcg)	Estrogen (mcg)	Remarks
Cyproterone/ Ethinyl estradiol[1]	2000	35	**Adverse Reactions** • Minor side effects occur during the 1st 3 cycles (nausea, breast tenderness, headache); Irregular menstrual bleeding (breakthrough bleeding or spotting most likely, amenorrhea in 2% to 3% of cycles); Other effects (acne, mood changes) • Relative risk of VTE can increase w/ COC use but risk is still low & considerably lower than VTE risk associated w/ pregnancy • COC users w/ hypertension or those who smoke ≥15 cigarettes/day have an increased relative risk of MI & stroke **Special Instructions** • COCs should not be used in women w/ known contraindication to the estrogen component or where the risks usually outweigh the advantages • Complete medical history should be done to check for risk factors of thrombus formation
Drospirenone/ Ethinyl estradiol	3000	20	
Levonorgestrel/ Ethinyl estradiol[2]	150	30	
	125	30	

[1]Cyproterone/Ethinyl estradiol should be taken as recommended for approved indication.
[2]Combination w/ Ferrous fumarate is available. Please see the latest MIMS for specific prescribing information.

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Dosage Guidelines

DIURETICS		
Drug	**Dosage**	**Remarks**
Hydro-chlorothiazide	25-100 mg PO 24 hrly	**Adverse Reactions:** • Metabolic effects (hyperglycemia, glycosuria in susceptible patients, hyperuricemia, hypokalemia); GI effects (GI upset, N/V, diarrhea); Hypersensitivity reactions **Special Instructions** • Use w/ caution in patients w/ renal impairment, existing fluid & electrolyte disturbances; may precipitate attacks of gout, cause hyperglycemia & aggravate or unmask DM • Avoid in patients w/ severe renal impairment or anuria, Addison's disease, preexisting hypercalcemia
Spironolactone	100 mg PO 24 hrly during the luteal phase	**Adverse Reactions:** • CNS effects (headache, drowsiness, ataxia, mental confusion); GI effects (cramps, diarrhea); Endocrine & metabolic effects (gynecomastia, breast pain, hirsutism, mild acidosis, hyponatremia, hyperkalemia & transient increases in BUN) **Special Instructions** • Avoid in patients w/ hyperkalemia or severe renal impairment • Use w/ caution in patients at increased risk of developing hyperkalemia

DOPAMINE AGONIST		
Drug	**Dosage**	**Remarks**
Bromocriptine	2.5 mg PO 12 hrly initiated 10 to 14 days prior to menses & discontinued when menses begins	**Adverse Reactions** • GI effects (N/V); CNS effects (dizziness, headache, syncope may occur, very rarely seizures); CV effects (digital vasospasm, leg cramps, orthostatic hypotension, severe hypotension, arrhythmia, chest pain; very rarely hypertension, MI, stroke) **Special Precautions** • Take w/ food to minimize nausea • Use w/ caution in patients w/ CV disease, psychiatric disorders

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Dosage Guidelines

GONADOTROPIN RELEASING HORMONE ANALOGUES		
Drug	**Dosage**	**Remarks**
Buserelin (Buserelin acetate)	1 spray (0.15 mg) into each nostril 8 hrly **Total daily dose:** 0.9 mg/day **Duration:** 6 mth	**Adverse Reactions** • Hypoestrogenism (manifests as transient vag bleeding, hot flushes, vag dryness, decreased libido, breast tenderness, insomnia, depression, irritability & fatigue, decreased elasticity of the skin, headache, after several wk of treatment: Osteoporosis); GI effects (nausea, abdominal discomfort); Other effects (transient increase in menstrual bleeding, reduction in glucose tolerance can develop, changes in serum lipids, hepatic effects & hypersensitivity reactions) **Special Instructions** • Addback strategy w/ estrogen/progesterone can eliminate most of these side effects • For nasal spray, avoid use of nasal decongestants before & for at least 30 min after treatment; repeat dose if sneezing occurs during or immediately after administration
Goserelin (Goserelin acetate)	3.6 mg depot inj SC into the anterior abdominal wall every 28 days **Duration:** 6 mth May increase duration when using estrogen/ progesterone addback	
Leuprorelin (Leuprorelin acetate)	3.75 mg depot inj SC/IM once mthly **Duration:** 6 mth May increase duration when using estrogen/ progesterone addback	
Nafarelin	1 spray (200 mcg) in 1 nostril in the morning & 1 spray (200 mcg) in the other nostril in the evening Start on days 2-4 of menstruation **Total daily dose:** 400 mcg/day **Duration:** 6 mth	
Triptorelin	3.75 mg depot inj SC/ IM once every 28 days **Duration:** 6 mth	

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Dosage Guidelines

PROGESTOGENS (ORAL)

Drug	Dosage	Remarks
Dydrogesterone	10 mg PO 12 hrly from days 11-25 of the menstrual cycle **Duration:** 3-6 mth	**Adverse Reactions** • CNS effects (headache, migraine); GI effects (GI upset, abdominal pain, change in wt/appetite); Breast changes (enlargement, secretion, discomfort); Dermatologic effects (allergic rash w/ or w/o pruritus, chloasma); Gynecological effects (changes in cervical secretions, vag infection); Hepatic effects (change in liver function, jaundice) rarely occur; Other effects (fluid retention, edema, alterations in lipid profile, reduced glucose tolerance) • Increase in size of leiomyomata & androgenic effects (acne, mental depression, changes in libido, hair loss, hirsutism, intermenstrual bleeding) are more common in Norethisterone **Special Instructions** • Patient should have regular breast exams • Should not be used if woman is pregnant, experiencing unexplained vag bleeding, has known or suspected breast cancer, history or current high risk of arterial disease, severe hepatic impairment • Use w/ caution in women w/ HTN, DM, asthma, hyperlipidemias, migraine, depression, cardiac or renal impairment, arterial/venous thromboembolism, or other conditions which may be aggravated by fluid retention
Lynestrenol	5 mg PO 24 hrly from days 16-25 of the menstrual cycle	
Nomegestrol acetate	5 mg PO 24 hrly for 10 days/cycle (from the 15th to 24th day)	
Norethisterone	5-15 mg PO 24 hrly from days 16-25 of the menstrual cycle	
Progesterone	200-300 mg PO divided 12-24 hrly	

PROGESTOGEN (RECTAL)

Drug	Available Strength	Dosage	Remarks
Progesterone	200 mg/pessary or suppository 400 mg/pessary or suppository	200 mg rectal 24 hrly to 400 mg rectal 12 hrly, start on day 14 of menstrual cycle & continue until onset of menstruation. Start on day 12 if symptoms are present at ovulation	**Adverse Reactions** • CNS effects (headache, somnolence, nervousness); GI effects (N/V, abdominal pain); Breast changes (enlargement, discomfort); Gynecological effects (changes in cervical secretions, vag bleeding, vag infection); Other effects (fluid retention, edema, arthralgia) **Special Instructions** • Patient should have regular breast exams • Should not be used if woman is pregnant, experiencing unexplained vag bleeding, or known or suspected breast cancer • Use w/ caution in women w/ DM, asthma, migraine, cardiac or renal impairment, or other conditions which may be aggravated by fluid retention

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Dosage Guidelines

PROGESTOGEN (VAGINAL)			
Drug	**Available Strength**	**Dosage**	**Remarks**
Progesterone	200 mg/pessary or suppository 400 mg/pessary or suppository	200 mg vag 24 hrly to 400 mg vag 12 hrly, start on day 14 of menstrual cycle & continue until onset of menstruation. Start on day 12 if symptoms are present at ovulation	**Adverse Reactions** • CNS effects (headache, somnolence, nervousness); GI effects (N/V, abdominal pain); Breast changes (enlargement, discomfort); Gynecological effects (changes in cervical secretions, vaginal bleeding, vaginal infection); Other effects (fluid retention, edema, arthralgia) **Special Instructions** • Patient should have regular breast exams • Should not be used if woman is pregnant, experiencing unexplained vaginal bleeding, or known or suspected breast cancer • Use w/ caution in women w/ DM, asthma, migraine, cardiac or renal impairment, or other conditions which may be aggravated by fluid retention

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)		
Drug	**Dosage**	**Remarks**
Citalopram	20 mg PO 24 hrly continuously or during luteal phase only	**Adverse Reactions** • CNS effects (insomnia, somnolence, nervousness, anxiety, headache, dizziness, fatigue, tremors; paresthesia & agitation are more common in Sertraline); GI effects (xerostomia, nausea, constipation, diarrhea, anorexia); Other effects (sexual dysfunction, mania, abnormal dreams, increased sweating, abnormal vision) **Special Instructions** • Observe patient for clinical worsening & suicidality • Use w/ caution in patients w/ hepatic or renal dysfunction & in patients w/ seizure disorders
Escitalopram	10-20 mg PO 24 hrly continuously or during luteal phase only	
Fluoxetine	20 mg PO 24 hrly continuously or during luteal phase only	
Paroxetine	**Extended-release:** 12.5 mg PO 24 hrly starting 14 days prior to the expected onset of menses, & terminating on the 1st day of menses May increase to 25 mg/day in 12.5-mg/day increments at intervals of at least 1 wk	
Sertraline	50-150 mg PO 24 hrly throughout the menstrual cycle or during luteal phase only May increase to 150 mg/day (at 50-mg increments/menstrual cycle) or 100 mg/day during luteal phase	

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Dosage Guidelines

OTHER ANTIDEPRESSANTS		
Drug	**Dosage**	**Remarks**
Clomipramine	25-75 mg PO 24 hrly continuously or for luteal phase only	**Adverse Reactions** • Antimuscarinic effects (xerostomia, constipation, urinary retention, accommodation disturbances, hyperthermia); CNS effects (dizziness, drowsiness, headache, insomnia, nervousness); GI effects (appetite increased, N/V, wt gain, dyspepsia, anorexia, abdominal pain); Endocrine effect (libido changes); Other effects (diaphoresis, fatigue, tremors) **Special Precautions** • Observe patient for clinical worsening & suicidality • Use w/ caution in patients w/ CV, hepatic & renal disease, & in patients receiving thyroid supplements
Venlafaxine	37.5-75 mg PO 12 hrly **Max dose:** 375 mg/day	**Adverse Reactions** • GI effects (N/V, anorexia, dry mouth, constipation, dyspepsia, hepatic impairment); CNS effects (tremor, anxiety, dizziness, headache, syncope, insomnia, somnolence, aggressive behavior); CV effect (orthostatic hypotension); Hematologic effects (hyponatremia, blood dyscrasias); Other effects (Stevens-Johnson syndrome, sweating, rash, fatigue, sexual dysfunction, visual disturbances) **Special Precautions** • Observe patient for symptoms of psychomotor restlessness & neuroleptic malignant syndrome • Use w/ caution in elderly patients & those w/ hepatic or renal disease, history of MI, bleeding disorder, epilepsy, hypomania or mania, increased intraocular pressure, & hypovolemia

OTHER DRUGS AFFECTING HORMONAL REGULATION		
Drug	**Dosage**	**Remarks**
Black cohosh (*Cimcifuga racemosa*) rhizome extr	20-40 mg PO 12-24 hrly	**Adverse Reactions** • Rarely may cause GI disturbances, hepatitis, myopathy **Special Instructions** • Should be taken w/ food • Use w/ caution in patients w/ history of liver disease

SUPPLEMENTS & ADJUVANT THERAPY		
Drug	**Dosage**	**Remarks**
Evening primrose oil[1]	1000 mg PO 8-24 hrly	**Special Precautions** • Should be taken w/ food

[1]Various combination products are available. Please see the latest MIMS for specific formulations & prescribing information.

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