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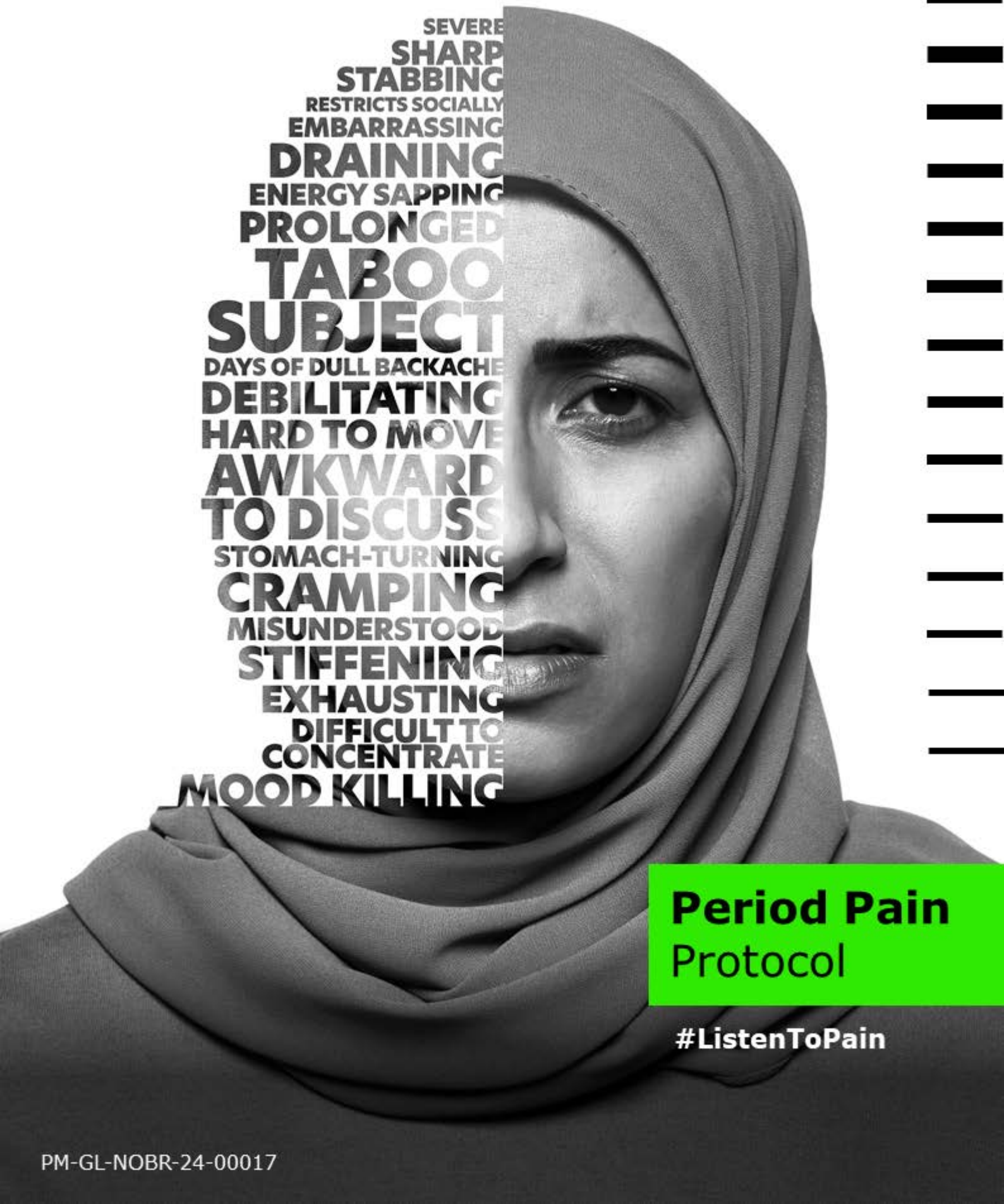

Period Pain Protocol

#ListenToPain

PM-GL-NOBR-24-00017

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DYSMENORRHEA (PERIOD PAIN) PROTOCOL IN PRIMARY CARE SETTINGS

STEP 1: ASSESS PERIOD PAIN

1. ASK PATIENT ABOUT PERIOD PAIN SYMPTOMS[1-3]

Type of pain (Cramping/ colicky/intense/ constant or sporadic)	Location (lower abdomen radiating to the back)	Onset of pain (pain starts shortly before or after menses)	Lethargy/ Fatigue/ dizziness	Muscle cramps	Associated symptoms (anxiety/ depression, nausea)

2. IDENTIFY SYMPTOMS OR CIRCUMSTANCES REQUIRING REFERRAL[1,4]

Severe dysmenorrhea immediately after menarche or progressively worsening dysmenorrhea	Lack of response to empiric medical treatment
Abnormal uterine bleeding (both heavy menstrual bleeding and irregular bleeding)	Family history of endometriosis
Mid-cycle or acyclic pain	Renal anomaly
Dyspareunia (persistent pain in the genital area during or after sexual intercourse)	Other congenital anomalies (spine, cardiac, or gastrointestinal)

STEP 2: IDENTIFY TREATMENT CONSIDERATIONS

IDENTIFY ANY CONDITIONS OR MEDICATIONS LIMITING TREATMENT OPTIONS[5-9]

Medications limiting treatment	Medical conditions limiting treatment
• **NSAIDs*** – Risk of bleeding, decreased antihypertensive efficacy, increased drug levels of medicines like methotrexate • **Paracetamol** -Increased risk of paracetamol toxicity	• Chronic kidney disease • Liver disease • Peptic Ulcer disease • Cardiovascular Disease

**** With oral NSAIDs only***

IDENTIFY WHAT THE PATIENT HAS USED IN THE PAST TO TREAT THE PAIN

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STEP 3: RECOMMEND TREATMENT FOR PERIOD PAIN (APPARENTLY UNCOMPLICATED ACUTE PERIOD)

DOES THE PATIENT HAVE ANY PREFERENCE FOR TREATMENT BASED ON WHAT WAS USED IN THEPAST ?

IF YES

Recommend non-pharmacological treatment[1,2, 10,11]

- Regular exercise (walking, jogging, low intensity yoga)
- Complementary or alternative treatment
  - Local heat in the form of heated pads (applied to lower abdomen)
  - High-frequency transcutaneous electrical nerve stimulation-TENS (*Involves the use of electrodes to stimulate the skin at various frequencies and intensities in an attempt to diminish pain perception)*
  - Acupoint stimulation (acupressure and acupuncture)
  - Relaxation training
  - Dietary supplements like ginger, fenugreek etc.

AND

Recommend the PATIENT's preference if possible, taking into consideration step 2

IF NO

Recommend non-pharmacological treatment[1,2,10,11]

- Regular exercise (walking, jogging, low intensity yoga)
- Complementary or alternative treatment
  - Local heat in the form of heated pads (applied to lower abdomen)
  - High-frequency transcutaneous electrical nerve stimulation-TENS (*Involves the use of electrodes to stimulate the skin at various frequencies and intensities in an attempt to diminish pain perception)*
  - Acupoint stimulation (acupressure and acupuncture)
  - Relaxation training
  - Dietary supplements like ginger, fenugreek etc.

AND

Recommend appropriate treatment for PERIOD PAIN[1,2,10]

Non-hormonal therapies:[1,2, 10]

- **Ibuprofen** 800 mg initially, followed by 400-800 mg every 8 hours as needed
- **Naproxen**: 440-550 initially, followed by 220-550 mg every 12 hours as needed
- **Mefenamic acid:** 500 mg initially, followed by 250 mg every 6 hours as needed
- **Celecoxib** (for females older than 18 years old): 400 mg initially, followed by 200 mg every 12 hours as needed
- **Paracetamol:** 500-1000 mg every 4-6 hours (max. dose 4gm/day)

Hormonal agents (if NSAIDs do not provide adequate relief of symptoms)[1,2, 10]

- Combined hormonal contraceptives (CHC) with 20-35 µg ethinyl estradiol
- Progestin-only-contraceptives
- Contraceptive transdermal patches or vaginal ring

ADULT ACUTE PERIOD PAIN PROTOCOL IN PRIMARY CARE SETTINGS

STEP 1

ASSESS SYMPTOMS

- Questions to ask (Table 1)
- Assess type of period pain (Primary Vs Secondary) (Table 2)
- Symptoms or circumstances requiring referral (Table 3)

Note: Patients with a presumed diagnosis of primary dysmenorrhea should be monitored for response to treatment. Tools that can be used for assessing dysmenorrhea at initial presentation as well as in response to treatment include visual analog scales and numerical rating scales.[1]

When a patient does not experience clinical improvement for her dysmenorrhea within 3–6 months of therapy initiation, possible secondary causes and treatment adherence should be investigated.[1]

STEP 2

IDENTIFY TREATMENT CONSIDERATIONS

- Questions to ask to customize treatment (Table 4)
- Conditions and medications (Tables 5 and 6)
- Assess previous treatment (Table 7)
- Questions to ask about previous treatment (Table 7)

STEP 3

RECOMMEND TREATMENT

- Non-pharmacological recommendations (Table 8)
- Pharmacological recommendation (Table 9)

STEP 1: ASSESS SYMPTOMS

TABLE 1

QUESTIONS TO ASK
Can you tell me about your period pain symptoms?[2,10] • Is the pain cramping in nature? • Does it radiate to the inner thigh or back? • Is the pain sporadic and intense or constant and dull? • Does the pain commence shortly prior to menstruation and continues for up to 72 hours, improving as menses progresses? • With the abdominal pain do you experience symptoms like nausea, vomiting, diarrhoea, fatigue, irritability, dizziness, bloating, headache, lower back pain and emotional symptoms? • Is there an increase or decrease in appetite with the period pain?
Other questions[2,10] • How long ago did menstruation begin and is the cycle regular? • When did menstruation become painful? • Are there any other symptoms? (depression, anxiety etc.) • Do the symptoms occur only during menstruation or also at other times of the cycle?

TABLE 2

CRITERIA FOR CLASSIFICATION OF PERIOD PAIN (Dysmenorrhea)[1]	
Primary Dysmenorrhea	**Secondary Dysmenorrhea**
• Painful menstruation in the absence of pelvic pathology • Pain characteristically begins when adolescents attain ovulatory cycles, usually within 6–12 months of menarche. • The pathophysiology is related to prostaglandins and leukotrienes, both mediators of inflammation.	• Painful menses due to pelvic pathology or a recognized medical condition. • Most common cause of secondary dysmenorrhea is endometriosis. • Other causes of secondary dysmenorrhea include: o Adenomyosis, infection, uterine myomas, müllerian anomalies, obstructive reproductive tract anomalies, uterine polyps or ovarian cysts.

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STEP 1: ASSESS SYMPTOMS

TABLE 3

SYMPTOMS OR CIRCUMSTANCES REQUIRING REFERRAL (RED FLAGS)	
Suspect secondary dysmenorrhea if the patient reports the following symptoms and refer them to a specialist.[1,4]	
Signs and symptoms	**Probable diagnosis/condition**
Infertility; pain with intercourse, urination, or bowel movements	Endometriosis
Sudden onset and resolution; if twisted, can cause ovarian torsion	Ovarian cysts
Irregular vaginal bleeding	Uterine polyps
Heavy, prolonged periods; constipation or difficulty emptying the bladder possible; more common in older people.	Uterine leiomyomas
Heavy bleeding, blood clots, pain with intercourse, abdominal tenderness; more common in older people	Adenomyosis
Abdominal pain, fever, vaginal discharge and odor, pain with intercourse, bleeding after intercourse	Pelvic inflammatory disease
History of surgery, infertility, bowel obstruction, painful bowel movements, pain with change in position	Pelvic adhesions
Bloating, frequent urination, nausea	Pelvic masses

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STEP 2:
IDENTIFY TREATMENT CONSIDERATIONS

TABLE 4

QUESTIONS TO ASK TO CUSTOMIZE PERIOD PAIN TREATMENT
• Are you taking any regular medicines, both on prescription and over-the-counter (OTC)? • Have you already taken any medicine to alleviate the symptoms?

TABLE 5

MEDICATIONS TO USE WITH CAUTION WITH PARACETAMOL/ORAL NSAIDS[5,12,13]

Concern	Potential drug interaction
Increased risk of bleeding with oral NSAIDs	• Some Selective-Serotonin Reuptake Inhibitors (SSRI) • Some tricyclic antidepressants • Acetylsalicylic acid (ASA) • Corticosteroids • Warfarin • Ginkgo biloba
Decreased antihypertensive efficacy with oral NSAIDs	• Angiotensin converting enzyme (ACE) inhibitors • Angiotensin II receptor blockers (ARB) • Diuretics • Beta-blockers
Increased drug levels with oral NSAIDs	• Lithium • Methotrexate
Increased risk of paracetamol toxicity	• Epilepsy medications (e.g. carbamazepine) • Other P450 enzyme inducers (e.g. isoniazid, rifampin) • Alcohol

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STEP 2:
IDENTIFY TREATMENT CONSIDERATIONS

TABLE 6

CONSIDERATIONS WHEN SELECTING ANALGESICS IN PATIENTS WITH COMORBIDITIES[5-9]

Comorbidity	Notes
Chronic kidney disease	• NSAIDs have proven nephrotoxic class effects and should be avoided where possible in patients with symptoms of renal impairment • Paracetamol is the preferred first-line analgesic for episodic treatment of mild pain in patients with renal dysfunction, CKD, and/or requiring dialysis. However, dose minimization may sometimes be warranted (maximum of 3 g/day has been recommended for patients with advanced kidney failure)
Liver disease	• NSAIDs- NSAIDs can cause acute liver injury with variable severity. • Paracetamol: Not contraindicated in liver disease. Can cause liver toxicity if taken in large amounts.
Peptic-ulcer disease	• Chronic NSAID drug use is associated with potentially serious upper gastrointestinal adverse drug reactions including peptic ulcer disease and gastrointestinal bleeding. • Paracetamol – Lesser risk of adverse effects compared to NSAIDs
Cardiovascular disease	• All non-aspirin NSAIDs may be associated with a potential increase in CV thrombotic risk. • NSAIDs are contraindicated in patients who have undergone coronary artery bypass graft surgery • Use of paracetamol at recommended doses is not associated with any additional risk of major CV events.

TABLE 7

QUESTIONS TO ASK TO ABOUT PREVIOUS TREATMENT

- What have you used before to treat your period pain?
  - What dose did you use?
  - Was it effective?
  - Did you have any side effects from it?
- Do you have any preference for any specific treatment?
- Have you used any alternative treatments to relieve period pain?

STEP 3: RECOMMEND TREATMENT

TABLE 8

NON-PHARMACOLOGICAL RECOMMENDATIONS FOR PERIOD PAIN[1,2]

- Regular exercise is likely to improve symptoms of dysmenorrhea and should be recommended
- Complementary or alternative treatment
  - Local heat in the form of heated pads or patches (applied to lower abdomen)
  - High-frequency transcutaneous electrical nerve stimulation-TENS (*Involves the use of electrodes to stimulate the skin at various frequencies and intensities in an attempt to diminish pain perception)*
  - Acupoint stimulation (acupressure and acupuncture)
  - Relaxation training
  - Dietary supplements for which there may be limited evidence to suggest a potential benefit include ginger, fenugreek, fish oil, fish oil plus vitamin B1, valerian, vitamin B1 alone, zataria, and zinc sulphate

TABLE 9

RECOMMENDATIONS FOR THE PHARMACOLOGIC MANAGEMENT OF PERIOD PAIN (PRIMARY DYSMENORRHEA)[1-3,5-10,14,15, 16]

Medication	Adverse Events	Drug Interactions	Comments
Non-steroidal anti-inflammatory drugs (NSAIDs) **Ibuprofen** • 800 mg initially, followed by 400-800 mg every 8 hours as needed **Naproxen** • 440-550 initially, followed by 220-550 mg every 12 hours as needed **Mefenamic acid** 500 mg initially, followed by 250 mg every 6 hours as needed **Celecoxib (COX-2 inhibitor): for females older than 18 years old** 400 mg initially, followed by 200 mg every 12 hours as needed	NSAID increase the risk of GI problems (ulceration, bleeding, and stomach/intestinal perforation) Contraindicated in those with hypersensitivity to NSAIDs including aspirin, patients with history of peptic ulcer or GI bleeding or those undergoing a coronary artery bypass grafting (CABG) Use with caution in patients with heart and kidney disease, liver cirrhosis, high blood pressure, uncontrolled diabetes, glaucoma asthma, urinary incontinence or an enlarged prostate.	Decreases the effect of diuretics like thiazide and furosemide, and ACE inhibitors like lisinopril and captopril Reduces the effect on platelets, including the impact of low dose aspirin. Take aspirin at least 30 mins before taking ibuprofen or naproxen Adverse effects may be increased when used along with medications like warfarin and aspirin, and antidepressant SSRIs like sertraline, fluoxetine etc.	Most effective when started 1–2 days before the onset of menses and continued through the first 2–3 days of bleeding. Taking the medication with food and increasing fluid intake may mitigate gastrointestinal and renal adverse effects.

TABLE 9 CONT.

STEP 3: RECOMMEND TREATMENT

TABLE 9 CONT.

Paracetamol 500-1000 mg every 4-6 hours (max. dose 4gm/day)	Good safety profile at therapeutic levels. Can cause liver toxicity if taken in large amounts. Dosage must be appropriately adjusted/lowered for poorly nourished patients, those with liver dysfunction, or those undergoing treatment with other hepatotoxic medications. Dose reduction may be needed in severe renal impairment and hepatic disease	Paracetamol + isoniazid: may increase the risk of hepatotoxicity Paracetamol + imatinib: may increase levels of paracetamol Paracetamol + warfarin: may increase the risk of bleeding.	Analgesic of choice for dysmenorrhea patients who do not desire hormonal contraceptives and cannot tolerate NSAIDs for their gastrointestinal disturbance.
Hormonal contraceptives Combined hormonal contraceptives (CHC) with 20-35 µg ethinyl estradiol Progestin-only-contraceptives [Progestin implant, intramuscular or subcutaneous depot medroxyprogesterone acetate, and levonorgestrel-releasing intrauterine system (LNG-IUS 52-mg)] Contraceptive transdermal patches or vaginal ring	Most common adverse effect of CHC: Breakthrough bleeding. Other adverse effects: Nausea, headaches, abdominal cramping, breast tenderness, and increased vaginal discharge or decreased libido. Nausea can be avoided by taking the medication at night before sleep. Women who have a pre-existing cardiovascular condition or smoke should not use oral contraceptives.	Antiepileptics such as carbamazepine, topiramate and phenytoin decrease contraceptive effectiveness of OCPs, whereas the use of lamotrigine and an OCP increases metabolism of lamotrigine. Certain antibiotics more likely to reduce OCP effectiveness include azithromycin erythromycin, ketoconazole, penicillin (and derivatives), rifampin, rifabutin and tetracycline antibiotics.	Hormonal contraceptives are usually recommended for dysmenorrhea females who need contraception, for whom the use of contraceptives is acceptable, or for those who cannot tolerate or are not responsive to NSAIDs. Continuous and extended use of CHC regimens is superior to cyclical regimens for pain relief. Continuous oral progestin is useful as an alternative to CHC with comparable pain relief and fewer side effects.
Nonsteroidal anti-inflammatory drugs may be continued or added to hormonal therapy as needed.			

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