PHARMACY PHACTS

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Risks with NSAIDs

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Nonsteroidal anti-inflammatory drugs (NSAIDs) are indicated for management of fever, pain and inflammation. With prolonged use, however, these medications can potentially pose significant risks that may affect patient's renal, gastrointestinal and cardiovascular health. NSAIDS can impair renal function by reducing kidney perfusion.[1] As a consequence, fluid retention is the most common renal complication seen.[2,3] This can in turn lead to hypertension and electrolyte imbalances such as hyperkalemia.[5] In rare cases, acute renal failure can also result from NSAID-induced renal ischemia.[1] As a consequence, patients present with symptoms of edema, weight gain, or electrolyte imbalances.

Gastrointestinal (GI) side effects are commonly (15-60%) seen with NSAIDs. The risk of GI problems such as GI bleeds, heartburn, nausea/vomiting, and ulcers increases in older patients who take NSAIDs regularly. Other factors include history of stomach ulcers, current anticoagulation, or corticosteroid treatment.

Alcohol use can also increase the risk of GI complications.[1,2] The risk of GI bleed is lower in patients who use NSAIDs intermittently. To minimize risks, NSAIDs should be taken with food.[2] Other strategies include using NSAIDs such as naproxen, switching to a selective COX-2 inhibitor, switching route of administration to diclofenac gel or adding a proton pump inhibitor with NSAID administration.

All NSAIDs, except aspirin, pose a low but measurable risk of heart attack or stroke.[2] According to the FDA, this serious side effect can occur during the first weeks of NSAID use. Patients with a history of heart attack or other risk factors for cardiac events are most likely to experience this. Research has also shown that the risk appears to be more significant with higher doses of NSAIDs. In a systematic review, multiple papers evaluated the risk of cardiac events in four NSAIDs; diclofenac, ibuprofen, celecoxib and naproxen.[1,4] Only naproxen demonstrated a low to negligible risk for heart attacks or stroke, while celecoxib seemed to have the greatest risk.[3-5]

References provided on request.

Drug Interaction Review:
Carbamazepine and Hormonal Contraceptives

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Carbamazepine and other anti-epileptic drugs (AEDs) are widely prescribed for indications beyond epilepsy including neuropathic pain, migraine treatment, general anxiety disorder, and bipolar disorder. For the subpopulation of child-bearing women who are concomitantly prescribed AEDs and hormonal contraception, the possibility of a bi-directional interaction and subsequent therapeutic failure of either treatment becomes a clinically significant consideration. Patients may be faced with the risk of both breakthrough seizures and unintended pregnancy with this combination. Further, the teratogenicity of AEDs and the impact of seizure activity on the developing fetus poses great harm. This underscores the responsibility of health care professionals to provide continuous education to patients regarding AED therapy and hormonal contraceptive methods of choice.

Although a number of mechanisms underlie the bi-directional interactions between hormonal contraceptives and AEDs, the interaction with carbamazepine and other potent enzyme-inducing agents is secondary to accelerated metabolism of ethinyl estradiol and progestin and an ultimate decrease in contraceptive efficacy. Phenobarbital, phenytoin, and carbamazepine may also cause elevations in sex hormone-binding globulin (SHBG), which can lead to reduced progestin free plasma concentrations. (Table 1)

These pharmacokinetic interactions have the potential to decrease efficacy of combined hormonal contraceptives, contraceptive patches, and vaginal rings. Because enzyme-inducing AEDs also induce the metabolism of progestin, progestin-only pills (POPs), subdermal progestin implants, and emergency contraception should not be regarded as effective methods. Although limited evidence exists to guide management of these interactions, current clinical guidance is provided in Table 2. Induction of hepatic enzymes persists for as long as 4 weeks following discontinuation of the AED; thus, alternative contraceptive methods should be continued for up to 4 weeks even after the offending drug is stopped.

Table 1: Bi-directional Interactions between Hormonal Contraceptives and Select AEDs*

	AED may be reduced by COC^	Ethinyl estradiol may be reduced by AED	Progestin may be reduced by AED
Carbamazepine	No Data	Yes	Yes
Oxcarbazepine	No Data	Yes	Yes
Gabapentin	No Data	No	No
Lamotrigine	Yes	No	Yes
Levetiracetam	No	No	No
Phenytoin	No Data	Yes	Yes
Pregabalin	No Data	No Data	No Data
Topiramate	No Data	Yes#	No
Valproate	Yes	No	No

Dose dependent
^Combined oral contraceptive

*Adapted from Table 2 in Reimers A, et al.Seizure. 2015;28:66-70.

Table 2: Alternative Contraceptive Methods*

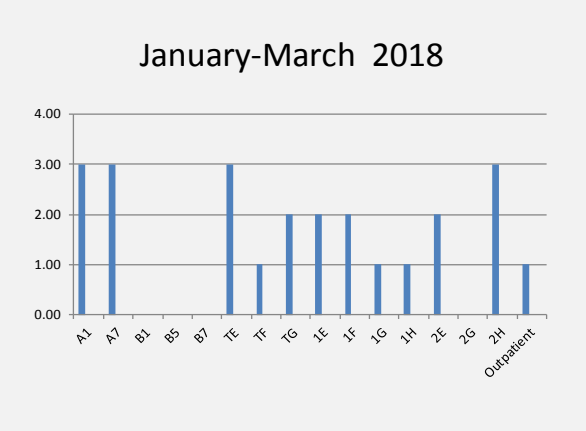
Method	Recommendations
Long-Acting	Depo-Provera Injection: Increased frequency (every 10 weeks rather than every 3 months) may be considered Levonorgestrel IUD Copper IUD
Barrier	Condom, female condom, diaphragm, contraceptive sponge
COC with ethinyl estradiol (EE) ≥50 mcg^	Consider increasing to EE 75-100 mcg if breakthrough bleeding occurs Consider tricycling or extended-cycle regimen Mestranol 50 mcg: not recommended ^Contraceptive failure may still occur; additional barrier methods or spermicidal gel recommended
Emergency contraceptive#	Two 1.5 mg levonorgestrel (3 mg total) given immediately within 72-120 hours following unprotected intercourse. Consider copper IUD #No studies on dosage effectiveness; Recommendations are outside of product labeling recommendations.

*Taken directly from Williams, D. US Pharm. 2014;39(1):39-42.

References available upon request.

Adverse Drug Reactions (ADRs)

Number of ADRs reported



You may report an ADR by calling x3784 or entering the data into the Sunrise Allergies System.

Formulary changes

- Remove Terbinafine from formulary
  - Only 2 tablets used in over a year
- Rifaximin remains non-formulary
  - $38 per tablet; will only order if clinically necessary
  - In most cases, recommendation for use comes from outside GI specialist

Drug shortages

- Injection diluents:
  - SWFI: vials now available on both campuses (only diluent approved for Zyprexa and Geodon reconstitution)
  - Normal Saline: 250 and 500 mL bag shortage
- Fluphenazine injection