In the ne name of ALLAH

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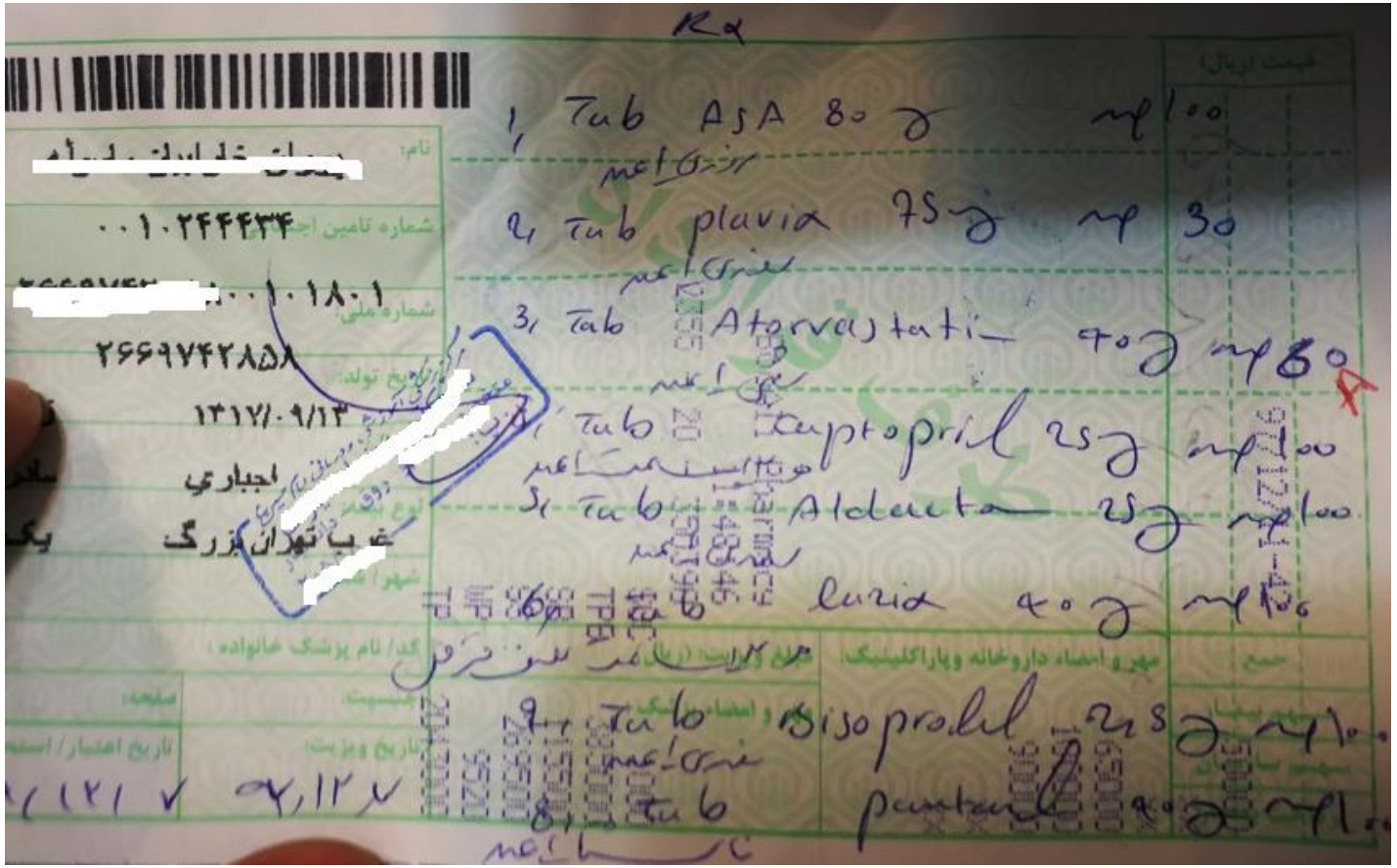
Principles of Prescribing in psychiatric medicine

تعریف نسخه

- نسخه یک سند حقوقی است و عبارت است از یک دستور دارویی که بطور کتبی یا شفاهی از طرف پزشک، دندانپزشک و یا سایر افرادی که مطابق قانون اجازه تجویز دارو را دارند، صادر می گردد و پزشک در برابر این سند حقوقی مسئولیت دارد.
- نسخه باید حاوی :
  - داروی معین (نوع دارو،شکل دارو، دوز، تعداد)
  - زمان مشخص
  - برای فرد به خصوص
- انواع نسخه:
  - کتبی
  - شفاهی
  - الکترونیک



درمورد هرقلم داروی تجویز شده بطورمعمول ۶ عامل باید مشخص گردد:

۱- نام دارو ۲- شکل دارو ۳- واحد داروئی ۴- تعداددارو ۵- نحوه مصرف ۶- فواصل تجویز

در نسخ الکترونیک حتما موارد فوق رعایت گردد.
اشتباهات در مواردی مانند تعداد، نحوه مصرف و فواصل تجویز شایع است.

نکات اصلی در تجویز دارو

- 1. به عنوان یک اصل، کمترین دارو برای کوتاه ترین دوره زمانی مورد نیاز تجویز شود.
- 2. طبق توصیه WHO ، میانگین اقلام کمتر، داروی تزریقی کمتر، داروی آنتی بیوتیک کمتر، استفاده از نام ژنریک و... جز موارد تجویز منطقی دارو به حساب می آید.
- 3. در کنار توصیات دارویی، حتما توصیات غیردارویی، آموزش به بیمار لحاظ شود.

Pharmacological Treatment of Mental Disorders in Primary Health Care

- **The decision** to prescribe a pharmacological treatment must take into consideration the potential risks and benefits to each individual patient. discuss with patients, family
- **Avoid poly pharmacy**
- **Consideration of other diseases** (TCA in depression and IBS)
- **Consideration of risk of Abuse**(Benzodiazepine in insomnia in previous opioid addicts)
- **Consideration of Adherence and monitoring**

- **Patients should be informed of possible side-effects**, and should also be informed about possible measures to manage them, i.e., reduction in the dose, reassurance that some of these side-effects are temporary (SSRIS after lunch)
- **Psychotropic drug discontinuation** should be done gradually (10-25% of the dose per week).
- Exception: fluoxetine (long half life)

P-Drugs

- P-drugs are the drugs you have chosen to prescribe regularly, and with which you have become familiar.

- Try to have the most updated, effective, safe and cheap P DRUGS !

Pharmacologic Therapy in Depression

- **First-line treatment** for a **moderate to-severe** depressive episode.

- Antidepressants have *equivalent efficacy* in groups of patients when administered in comparable doses.
- **Factors for drug section :** patient's **history of response**, history of familial antidepressant response, patient's concurrent medical illnesses and medications, presenting symptoms (eg, insomnia vs. hypersomnia), potential for drug–drug interactions, adverse event profile, patient preference, and medication cost

General Principles

- The patient should be informed that **adverse effects** might occur immediately, while symptoms of depression may take 2 to 4 weeks to improve and up to **3 months** for full resolution.
- **Adherence** to the treatment plan is essential for a successful outcome, and tools to help increase medication adherence should be discussed with each patient.
- **Newer generations of antidepressants:** such as the selective serotonin reuptake inhibitors (SSRIs), are equally effective and better tolerated (than older agents, such as the tricyclic antidepressants (TCAs) and the monoamine oxidase inhibitors (MAOIs).)

Compelling diseases

- **1.TCA:** neuropathic pain, migraine prophylaxis, IBS, fibromyalgia
- **2.SSRI /SNRI:** most of anxiety such as GAD, Panic attack ,...
- **Venlafaxine:** GAD/ migraine prophylaxis

Escitalopram and sertraline have the best combination of efficacy and acceptability

Selective Serotonin Reuptake Inhibitors

- SSRIs are generally chosen as ***first-line antidepressants*** due to their relative safety in overdose and improved tolerability over traditional TCAs and MAOIs.
- First choice for most types of anxiety

- The SSRIs, as the name implies, have **a low affinity** for other receptors including α_1-adrenergic, histaminic (H1), and muscarinic (M1) receptors

- **Differences in drug interaction profile and pharmacokinetic** (PK) parameters (eg, half-life).

Side Effects

- **Dose-dependent :** generally, are mild and limited to 1 to 2 weeks after initiation or dose increases, are gastrointestinal (GI) symptoms (eg, nausea, vomiting, and diarrhea), anxiety, and headache.
- **Both somnolence and insomnia** have been reported with all SSRIs (**Paroxetine and fluvoxamine** may cause somnolence).
- **Sexual Disorders**: including(arousal, libido, orgasm) however it is important to note that depression itself may be associated with sexual dysfunction. USE IN PREMATURE EJACULATION
- SIADH, Vivid dreams, tremor, **sweating ,anti platelet effect....**
- **Citalopram** to a dose dependent increase in QT interval. (>40mg/d)
- **Paroxetine** has more anticholinergic and antihistaminergic activity (sedation, dry mouth, anti pruritic ...)

Lithium Carbonate: Tab 300 mg, Tab SR 400 mg

- Chronic lithium administration may modulate **gene expression** and have **neuroprotective** effects.
- Lithium is a monovalent cation that is **rapidly absorbed**, and widely distributed with no protein binding. It is also not metabolized and is excreted unchanged in the urine and in other body fluids.
- **Efficacy:** Lithium is considered a first-line agent for acute mania acute bipolar depression, and maintenance treatment of bipolar I and II disorders and suicidal idea.

- **Slow Onset (1-2 week)**
- **Dose:** initial 600 mg then 900-2,400 mg/day in two to four divided doses, preferably **with meals**
- Renal impairment: lower doses required with frequent serum monitoring

- **TDM:** There is wide variation in the dosage needed to achieve therapeutic response and **trough serum lithium concentration** (ie, 0.6-1.2 mEq/L [mmol/L]

Side effect

- **Early:** Initial gastrointestinal (GI) and central nervous system (CNS) side effects (lowering the dose, taking doses with food, using extended-release products, and trying once-daily dosing at bedtime).
- Fine hand tremor can be evident in many patients while a course hand tremor may be a sign of toxicity. (switch to long-acting preparation, lower dose if possible) or adding a *β*-adrenergic antagonist).
- Polydipsia with polyuria : associated with or without nephrogenic diabetes insipidus (DI) which reversible with discontinuation of lithium .
- Hypothyroidism can occur in patients treated with lithium, occurring more frequently in women than men.
- **Supplemental exogenous thyroid hormone (ie, levothyroxine) can be added to the patients' regimen.**

- **OTHERS:**
  Acne and folliculitis (1%), reversible leukocytosis, and weight gain.
- Reversible cardiac effects, particularly t-wave flattening or inversion

- **Pregnancy and breastfeeding category** :
  XXXX

Benzodiazepine (GABA A agonist)

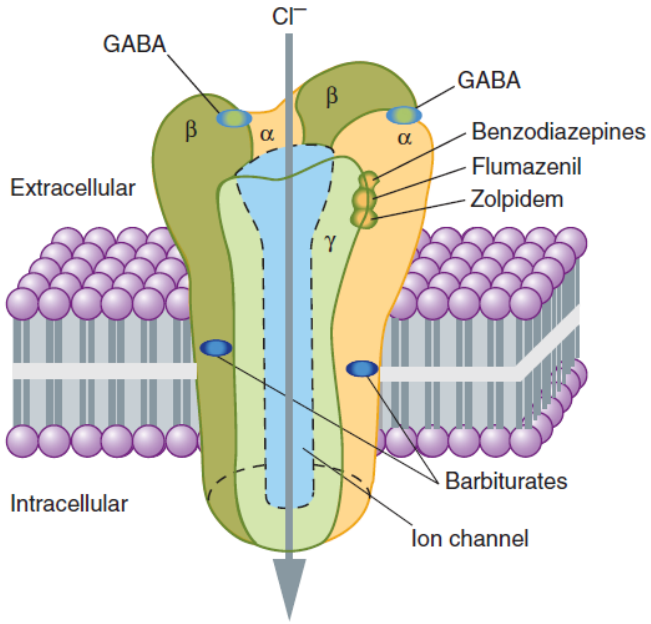


FIGURE 22–1 A model of the $GABA_A$ receptor-chloride ion channel macromolecular complex. A hetero-oligomeric glycopro-

Indications:

- **Acute stress, panic attack**
- **Insomnia:** including estazolam, flurazepam, and triazolam

- **Muscle relaxant**: diazepam/ clonazepam/ lorazepam
- **Withdrawal state (ethanol): l**onger acting benzodiazepines (eg, chlordiazepoxide, diazepam)
- **No metabolite** (good for elderly ang hepatic impairment): **oxazepam / lorazepam**

- **Clonazepam**: Tab 1, 2 mg (Relative Potency = 0.25)
- Potent/ panic attack /Anti seizure ,muscle relaxant
- **Alprazolam**: Tab 0.5, 1 mg, (Xanax®) (relative potency :0.5 mg)
- **Lorazepam**: Tab 1, 2 mg (Ativan®) (Relative Potency = 1)

Buspirone and Z hypnotic

- **Buspirone**: Tab 5, 10 mg (Buspar®)
- 5HT1 agonist/ indication: GAD, augmentation in depression
- Dose: 10-60mg/d

- **Zolpidem**: Tab 5, 10 mg (Stilnox, Zoldem®)
- Dose: 5 mg (women. elderly) – 10 mg / day
- **It had Better be used just before sleep with empty stomach**
- **Should limit the use for 4-8 weeks**
- **ADRS: risk of complex behavior (not fully awake but do some work!)/ hallucination/ risk of abuse**

- **Zaleplon:** tab 5,10 mg

Faster act than zolpidem

Drug Interaction

Pharmacokinetic interactions

Drug Absorption Interactions

Changes in GI pH:

- PPIs → ↓ketoconazole, levothyroxine, Iron absorption

Adsorption, chelation, complexing mechanisms:

- Bivalent and Trivalent cations (Iron, Calcium, Antacid,…) +Tetracycline, Fluroquinolone, Bisphosphonate

Changes in GI motility:

- Metoclopramide → ↓digoxin absorption

Drug metabolism interactions

Changes in first-pass metabolism

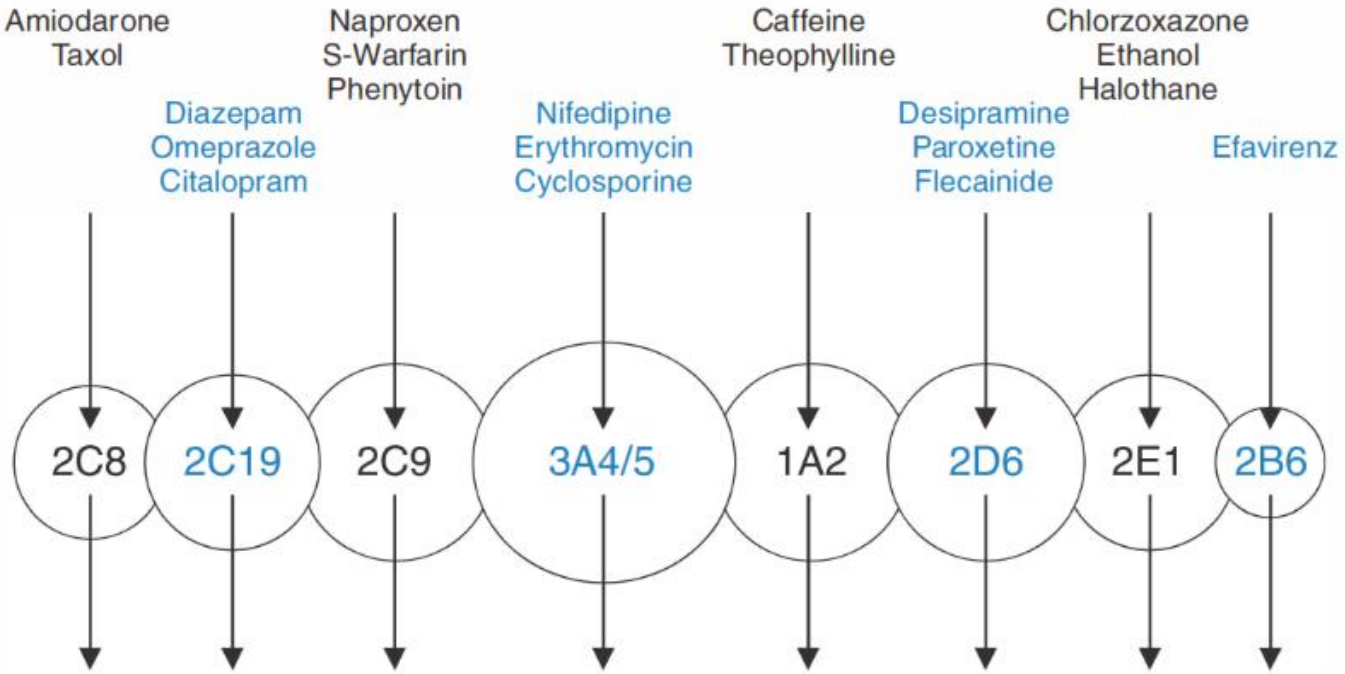
- *Changes in liver blood flow:* high-extraction β blockers with hydralazine
- *Inhibition/ induction of FPE:* the gut wall contains P450 isoenzymes

A. **Enzyme induction**
B. **Enzyme inhibition**

3A4 > 2D6

Genetic polymorphism: CYP2D6 slow metabolizers (5~10% in Caucasians, 0~2% in Asians and blacks)

SUBSTRATES



INHIBITORS

Gemfibrozil
Fluvoxamine
Fluconazole
Itraconazole
Clarithromycin
Ritonavir
Amiodarone
Quinidine
Paroxetine
Disulfiram

INDUCERS

Rifampin
Carbamazepine
Rifampin
Omeprazole
Ethanol
Rifampin

Pharmacodynamic interactions

Pharmacodynamic interactions

- **Additive or Synergism**
- **Antagonists**

Common Mechanisms of Pharmacodynamic Drug Interactions[65]

	Mechanism	Example
Pharmacodynamics	Additive—two or more medications with comparable pharmacodynamic effects result in an exaggerated and/or toxic response	Administration of thiopental and midazolam during induction. Midazolam reduces the amount of thiopental required for anesthesia
	Antagonistic—the effects of one drug oppose the actions of another drug	*Example 1:* Antagonism at the same receptor site: reversal of benzodiazepines with flumazenil. *Example 2:* Opposing pharmacodynamics actions: glucocorticoids cause hyperglycemia opposing the effects of hypoglycemic medications

Drug Interaction

TABLE 88-9 Select Pharmacokinetic Interactions of Antidepressants

Antidepressant	Interacting Medication/Medication Class	Effect
Selective Serotonin Reuptake Inhibitors		
Citalopram and escitalopram	Omeprazole	Increased concentrations of citalopram and escitalopram
Fluoxetine	Alprazolam	Increased concentrations and half-life of alprazolam; increased psychomotor impairment
	Antipsychotics (eg, aripiprazole, haloperidol)	Increased antipsychotic concentrations; increased extrapyramidal symptoms
	β-Adrenergic blockers	Increased metoprolol concentrations; increased bradycardia; possible heart block
	Carbamazepine	Increased concentrations of carbamazepine; symptoms of carbamazepine toxicity
	Phenytoin	Increased concentrations of phenytoin; symptoms of phenytoin toxicity
	Tamoxifen	Decreased conversion of tamoxifen to active metabolites
	TCAs	Markedly increased TCA concentrations; symptoms of TCA toxicity
	Thioridazine	Thioridazine C_{max} increased; prolonged QTc interval
Fluvoxamine	Alosetron	Increased alosetron AUC (sixfold) and half-life (threefold)
	Alprazolam	Increased AUC of alprazolam by 96%, increased alprazolam half-life by 71%; increased psychomotor impairment
	β-Adrenergic blockers	Fivefold increase in propranolol concentration; bradycardia and hypotension
	Carbamazepine	Increased concentrations of carbamazepine; symptoms of carbamazepine toxicity
	Clozapine	Increased clozapine concentrations; increased risk for seizures and orthostatic hypotension
	Diltiazem	Bradycardia
	Methadone	Increased methadone plasma concentrations; symptoms of methadone toxicity
	Ramelteon	Increased AUC (190-fold) and C_{max} (70-fold)
	TCAs	Increased TCA concentration; symptoms of TCA toxicity
	Theophylline and caffeine	Increased concentrations of theophylline or caffeine; symptoms of theophylline or caffeine toxicity
	Thioridazine	Thioridazine C_{max} increased; prolonged QTc interval
	Warfarin	Increased effect of warfarin
Paroxetine	Antipsychotics (eg, aripiprazole, haloperidol)	Increased antipsychotic concentrations; increased CNS and extrapyramidal symptoms
	β-Adrenergic blockers	Increased metoprolol concentrations; increased bradycardia; possible heart block
	Tamoxifen	Decreased conversion of tamoxifen to active metabolites
	TCAs	Markedly increased TCA concentrations; symptoms of TCA toxicity
	Thioridazine	Thioridazine C_{max} increased; prolonged QTc interval
Sertraline	Methadone	Increased methadone levels

Drug Interactions

Serotonin–Norepinephrine Reuptake Inhibitors		
Venlafaxine and desvenlafaxine	CYP3A4 inhibitors	May increase levels of venlafaxine and *O*-desmethylvenlafaxine especially in CYP2D6 poor metabolizers
Duloxetine	Metoprolol	May increase metoprolol levels twofold
	Tamoxifen	Decreased conversion of tamoxifen to active metabolites
	Thioridazine	Thioridazine C_{max} increased; prolonged QTc interval
Levomilnacipran	CYP3A4 inhibitors	Clinically relevant increases in levomilnacipran concentrations may occur
Mixed Serotonergic (Mixed 5-HT)		
Vilazodone	CYP3A4 inhibitors	Maximum vilazodone dose 20 mg with coadministration of potent CYP3A4 inhibitor
Vortioxetine	CYP2D6 inhibitors	May need to reduce vortioxetine dose by half with coadministration of potent CYP2D6 inhibitor
Serotonin and α-2-Adrenergic Antagonist		
Mirtazapine	Carbamazepine	Mirtazapine concentration decreased (60%)
Norepinephrine and Dopamine Reuptake Inhibitor		
Bupropion	Tamoxifen	Decreased conversion of tamoxifen to active metabolites

TABLE 88-10 Select Pharmacodynamic Medication Interactions of Antidepressants

Medication/ Medication Class	Antidepressants/ Antidepressant Class	Effect and Management
NSAIDs Aspirin Anticoagulants Antiplatelet agents	SSRIs, SNRIs, TCAs, trazodone, vilazodone, vortioxetine	• FDA warning for increased risk of bleeding • Number needed to harm with NSAIDs = 82 vs >700 with SSRI alone • Assess for baseline bleeding risk and monitor closely • Educate at risk patients regarding signs of bleeding • Consider histamine-2 (H_2) antagonist in high-risk patients
Triptans	MAOIs, SSRIs, and SNRIs	• FDA warning in labeling • Very low risk • Monitor for signs of serotonin syndrome when frequent high doses are used • Triptan toxicity possible when almotriptan, rizatriptan, sumatriptan, or zolmitriptan are combined with MAO inhibitors
Linezolid	All serotonergic antidepressants	• Linezolid is weak, reversible, nonselective, MAOI • FDA labeling recommends against use with other MAOIs and recommends discontinuing antidepressants if linezolid is started • Actual rate of serotonin syndrome with combination reported at <1% • Abrupt discontinuation of antidepressants can have negative consequences • If linezolid is indicated and patient is already on an antidepressant, monitor for signs of serotonin syndrome upon initiating combination • If patient is on short course of linezolid and in need of treatment for depression, consider postponing antidepressant initiation until course is complete
Tramadol	Bupropion, duloxetine, fluoxetine, paroxetine	• Decreased metabolism results in increased SNRI activity of tramadol • Rare cases of high dose tramadol combined with CYP2D6 inhibitors resulting in serotonin syndrome have been reported • Monitor for increased signs of serotonin syndrome and decreased analgesic response when combination is used

Thank You for your Attention