DRUG – 01

Risperidone

Risperidone is a second-generation antipsychotic medication used to treat a number of mental health disorders including schizophrenia, bipolar mania, psychosis, or as an adjunct in severe depression.

ADR –

- Back pain
- chest pain
- speech or vision problems
- sudden weakness or numbness in the face, arms, or legs
- Confusion
- dizziness
- drowsiness
- extreme thirst
- fast, shallow breathing
- fast, weak heartbeat
- headache

MOA –

The mechanism of action of risperidone, as with other drugs used to treat schizophrenia, is unknown. However, it has been proposed that the drugs therapeutic activity in schizophrenia is mediated through a combination of dopamine Type 2 (D2) and serotonin Type 2 (5HT2) receptor antagonism.

CONTRAINDICATION –

- Alzheimer disease or.
- Dehydration or.
- Heart attack, recent or history of or.
- Heart or blood vessel disease or.
- Heart failure, history of or.
- Heart rhythm problem, or a history of or.
- Hypotension (low blood pressure) or.

KINETICS –

Absorption

- Orally disintegrating tablets and oral solution are bioequivalent to tablets.
- Rapidly absorbed after oral administration.
- Peak plasma levels achieved within 1 hour.
- Linear pharmacokinetics.

Distribution

- Volume of distribution: 1-2 L/kg.
- Risperidone binds to albumin and alpha1-acid glycoprotein.
- Plasma protein binding:
    - For risperidone: 90%
    - For 9-hydroxyrisperidone: 77%

Metabolism

- CYP 2D6 is the enzyme that catalyses hydroxylation of risperidone to 9-hydroxyrisperidone.
- The metabolite 9-hydroxyrisperidone has similar pharmacological activity as risperidone.
- CYP 2D6 is subject to genetic polymorphism

Excretion

- Apparent half-life of risperidone:
    - 3 hours in extensive metabolizers
    - 20 hours in poor metabolizers
- Apparent half-life of 9-hydroxyrisperidone:
    - 21 hours in extensive metabolizers
    - 30 hours in poor metabolize

INTERACTION –

risperidone & escitalopram

escitalopram together with risperidone can increase the risk of an irregular heart rhythm that may be serious and potentially life-threatening, although it is a relatively rare side effect.

Lorazepam & risperidone

lorazepam together with risperidone may increase side effects such as dizziness, drowsiness, confusion, and difficulty concentrating. Some people, especially the elderly, may also experience impairment in thinking, judgment, and motor coordination.

clonazepam & risperidone

clonazepam together with risperidone may increase side effects such as dizziness, drowsiness, confusion, and difficulty concentrating. Some people, especially the elderly, may also experience impairment in thinking, judgment, and motor coordination.

DRUG – 02

Clarithromycin

Clarithromycin is a macrolide antibiotic used for the treatment of a wide variety of bacterial infections such as acute otitis, pharyngitis, tonsillitis, respiratory tract infections, uncomplicated skin infections, and helicobacter pylori infection.

MOA –

Clarithromycin is first metabolized to 14-OH clarithromycin, which is active and works synergistically with its parent compound. Like other macrolides, it then penetrates bacteria cell wall and reversibly binds to domain V of the 23S ribosomal RNA of the 50S subunit of the bacterial ribosome, blocking translocation of aminoacyl transfer-RNA and polypeptide synthesis. Clarithromycin also inhibits the hepatic microsomal CYP3A4 isoenzyme and P-glycoprotein, an energy-dependent drug efflux pump

PHRMACOKINETICS –

Absorption

Clarithromycin is well-absorbed, acid stable and may be taken with food.

Protein binding

~ 70% protein bound

Metabolism

Hepatic - predominantly metabolized by CYP3A4 resulting in numerous drug interactions

Half-life

3-4 hours

ADR –

- Feeling sick (nausea) Stick to simple meals and do not eat rich or spicy food while you're taking this medicine. ...
- Being sick (vomiting) Try taking small, frequent sips of water to avoid dehydration. ...
- Diarrhoea. ...
- Bloating and indigestion. ...
- Headaches. ...
- Difficulty sleeping (insomnia)

CONTRAINDICATION –

- ergotamine or dihydroergotamine, used to treat migraines.
- medicines for epilepsy, such as carbamazepine or phenytoin.

- theophylline for asthma.
- colchicine for gout.
- digoxin, for some heart problems

INTERACTION –

clarithromycin & fluticasone

Clarithromycin may significantly increase the absorption of fluticasone into the blood stream. You may be more likely to experience side effects such as swelling, weight gain, high blood pressure, high blood glucose, muscle weakness, depression, acne, thinning skin, stretch marks, easy bruising, bone density loss.

Clarithromycin & salmeterol

Clarithromycin may significantly increase the blood levels of salmeterol following oral inhalation. High blood levels of salmeterol can increase the risk of an irregular heart rhythm that may be serious and potentially life-threatening, although it is a relatively rare side effect.

ciprofloxacin & clarithromycin

ciprofloxacin together with clarithromycin can increase the risk of an irregular heart rhythm that may be serious and potentially life-threatening, although it is a relatively rare side effect.

DRUG – 03

Warfarin

Warfarin is a vitamin K antagonist used to treat venous thromboembolism, pulmonary embolism, thromboembolism with atrial fibrillation, thromboembolism with cardiac valve replacement, and thromboembolic events post myocardial infarction.

Mechanism of action of warfarin

Warfarin inhibits vitamin KO reductase, and thus limits the availability of vitamin K in the cyclic reaction. This thus reduces the coagulant activity of blood by reducing the production of vitamin K-dependent factors. The effect of warfarin can be overcome by administering vitamin K1 (phytonadione), either as medication or through the diet.

This makes vitamin KH2 available for carboxylation without the need for vitamin KO reductase. It can also be stored in the liver if given in large enough quantities, producing warfarin resistance in the patient for varying periods of time.

Pharmacokinetics of warfarin

Warfarin is a mixture of the R and S optical isomers in racemic proportions. The S-form is five times as potent as the R-form in inhibiting vitamin K activity. After being rapidly absorbed from the intestine, warfarin reaches peak blood concentrations in about 90 minutes from oral ingestion.

It has a half-life of 36-42 hours and circulates bound mainly to plasma albumin (99%) as well as small amounts of other plasma proteins until it is stored in the liver for further metabolism. Its maximum effect is observed up to 48 hours after administration. Its actions last for up to 5 days.

Warfarin is metabolized in the liver and kidneys, mostly by hydroxylation, with the inactive products being excreted through urine and feces.

ADR—

- Gas
- abdominal pain
- bloating
- change in the way things taste
- loss of hair
- feeling cold or having chills
- rash
- itching
- swelling of the face, throat, tongue, lips, or eyes
- hoarseness
- chest pain or pressure
- swelling of the hands, feet, ankles, or lower legs
- fever
- infection
- nausea
- vomiting
- Diarrhea
- extreme tiredness
- lack of energy
- loss of appetite
- pain in the upper right part of the stomach
- yellowing of the skin or eyes

- flu-like symptoms

CONTRAINDICATION –

- Previous history of intracranial haemorrhage
- Recent history of a major extracranial bleed without known cause
- History of peptic ulceration within the past three months. In these cases, it is recommended that the patient waits to begin warfarin therapy until treatment of peptic ulcer is completed.
- Recent history of repeated falling episodes with a patient at a higher risk for bleeds
- Likelihood of poor patient compliance due to dementia or cognitive impairment, particularly in cases when there is no available caretaker.
- Alcoholism, especially binge drinking
- Poorly controlled or untreated hypertension

INTERACTION –

warfarin & aspirin

warfarin together with aspirin may cause you to bleed more easily. You may need a dose adjustment based on your prothrombin time or International Normalized Ratio (INR). Call your doctor promptly if you have any unusual bleeding or bruising, vomiting, blood in your urine or stools, headache, dizziness, or weakness.

warfarin & clopidogrel

warfarin together with clopidogrel can increase the risk of bleeding complications. Call your doctor promptly if you experience any unusual bleeding or bruising, vomiting or coughing up blood, blood in your urine or stools, headache, dizziness, weakness, or swelling.

warfarin & acetaminophen

any unusual bleeding or bruising, or have other signs and symptoms of bleeding such as dizziness; light-headedness; red or black, tarry stools; coughing up or vomiting fresh or dried blood that looks like coffee grounds; severe headache; and weakness.

DRUG – 04

Estazolam

Estazolam is a benzodiazepine used for the short-term management of insomnia.

Estazolam is used for the short-term treatment of insomnia (difficulty falling asleep or staying asleep). Estazolam is in a class of medications called benzodiazepines. It works by slowing activity in the brain to allow sleep.

Mechanism of Action

Benzodiazepines bind non-specifically to benzodiazepine receptors, which affects affect muscle relaxation, anticonvulsant activity, motor coordination, and memory. As benzodiazepine receptors are thought to be coupled to gamma-aminobutyric acid-A ($GABA_A$) receptors, this enhances the effects GABA by increasing GABA affinity for the GABA receptor. Binding of the inhibitory neurotransmitter GABA to the site opens the chloride channel, resulting in a hyperpolarized cell membrane that prevents further excitation of the cell.

Pharmacokinetics

- ✓ Half-Life: 10-24 hr
- ✓ Duration: Variable
- ✓ Peak Plasma Time: 0.5-1.6 hr
- ✓ Protein Bound: 93%
- ✓ Metabolism: Hepatic
- ✓ Metabolites: Inactive
- ✓ Excretion: Urine
- ✓ Half-life elimination: 10-24 h, and peak action is 2 h

ADR –

- ➢ Dizziness (7-8%)
- ➢ Hypokinesia (7-8%)
- ➢ Abnormal coordination (4%)

- Hangover (3%)
- Abnormal thinking (2%)
- Flushing palpitation
- Hangover effect
- Euphoria
- Seizure
- Sleep disorder
- Rash
- Urticaria

CONTRAINDICATION –

Documentation of allergenic cross-reactivity for benzodiazepines is limited. However, because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty.

INTERACTION –

clonazepam & estazolam

clonazepam together with estazolam may increase side effects such as dizziness, drowsiness, confusion, and difficulty concentrating.

Alprazolam & estazolam

Alprazolam together with estazolam may increase side effects such as dizziness, drowsiness, confusion, and difficulty concentrating.