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An Overview on "Symptoms, Diagnosis and Drug Treatment for Psychiatric Disorder"

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HUMAN

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Keywords: Chlorpromazine; Triflupromazine; Thioridazine; Trifluoperazine; Fluphenazine

ABSTRACT

Psychosis is an abnormal condition of the human mind that results in difficulties determining what is real and what is not? Symptoms of psychosis mean false beliefs and seeing or hearing things that others do not see or hear. Other symptoms may include speech problems and behavior that is inappropriate for the situation. It may include sleep problems, social withdrawal, motivation problems, and daily activity. It may include different causes for psychosis-like mental illness, sleep problems, bipolar disorder, and habit of drug-like alcohol or cannabis, etc.

INTRODUCTION:

Psychosis is defined as characterized by an impaired relationship with reality. It is a symptom of a serious mental problem. Psychosis is an abnormal condition of the mind. Psychosis may exhibit personality changes and thought disorder[1]. Psychosis is a sign of a psychiatric disorder. Psychosis is a descriptive term for hallucination and delusion. The first-line treatment for many psychotic disorders is an anti-psychotic medication.

Types of psychosis[2]:

It includes;

- **Schizophrenia**
- **Schizoaffective disorder**
- **Brief psychotic disorder**:
- **Delusional disorder**
- **Bipolar psychosis**
- **Psychotic depression**
- **Postpartum (also called postnatal) psychosis**

Symptoms of psychosis[3]:

The classic signs and symptoms of psychosis are Hallucinations, Delusions, Disordered thinking, and Catatonia.

The milder, initial symptoms of psychosis might include:

- Feelings of suspicion
- General anxiety
- Distorted perceptions
- Depression
- Obsessive thinking

- Sleep problems

Causes of psychosis[4]:

- Genetics
- Brain changes
- Hormones/sleep

Antipsychotic drugs:

Antipsychotics are effective at reducing psychosis symptoms in psychiatric disorders such as Schizophrenia.

Classification:

1. **Phenothiazine:**

A. Aliphatic Sidechain: Chlorpromazine, Triflupromazine

B. Piperidine side chain:Thioridazine

C. Piperazine side chain:Trifluoperazine, Fluphenazine

2. **Butyrophenones:** Haloperidol, Trifluperidol, Penfluridol
3. **Thioxanthenes:** Flupenthixol
4. **Another heterocyclic:** Pimozide, Loxapine
5. **Atypical Antipsychotic**

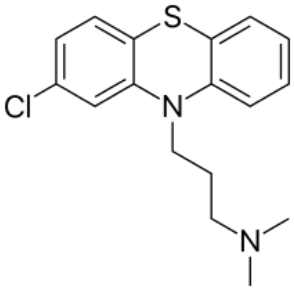
- Clozapine
- Risperidone
- Olanzapine
- Quetiapine
- Aripiprazole

- Ziprasidone
- Amisulpride
- Zotepine

1. Phenothiazine[5-9]:

A. Aliphatic Sidechain:

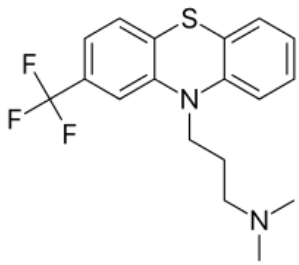
Chlorpromazine:



Systematic (IUPAC) name
• 3-(2-chloro-10*H*-phenothiazin-10-yl)-*N*,*N*-dimethyl-propan-1-amine

Chlorpromazine is also known as CPZ. Chlorpromazine is an example of an anti-psychotic drug. It is a derivative of Phenothiazine. It is available in the form of trade names like Thorazine and Largactil. It is primarily used to treat psychotic disorders like schizophrenia. It is also used to treat bipolar disorder, hyperactivity disorder. It is also used to treat nausea and vomiting. It can be given by mouth, intravenous, and intramuscular injection. It gives some side effects like movement problems, dry mouth, low blood pressure, and increased weight. Chlorpromazine was discovered in 1950 and was the first antipsychotic drug. Chlorpromazine is classified as a low-potency antipsychotic drug. It is used to treat acute and chronic psychosis. Chlorpromazine is occasionally used off-label for the treatment of severe migraine.

Triflupromazine:

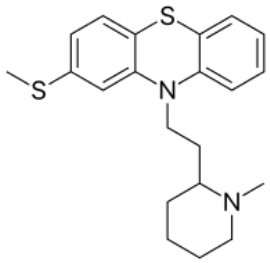


Systematic (IUPAC) name
• *N*,*N*-dimethyl-3-[2-(trifluoromethyl)-10*H*-phenothiazin-10-yl]propan-1-amine

Triflupromazine is an example of an anti-psychotic drug. It is a derivative of Phenothiazine. Triflupromazine is available in the form of trade name like Vesprin.

B. Piperidine side chain:

Thioridazine:

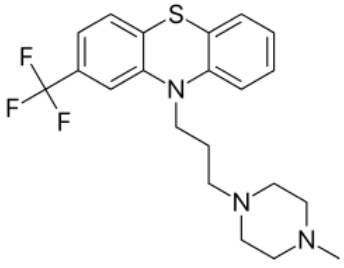


Systematic (IUPAC) name
• 10-{2-[(*RS*)-1-Methylpiperidin-2-yl]ethyl}- 2-methyl sulfanyl phenothiazine

Thioridazine is an example of piperidine typical antipsychotic drug belonging to the Phenothiazine category. Thioridazine was previously widely used in the treatment of schizophrenia and psychosis. Thioridazine is available in the form of racemic compounds like (*S*)- and (*R*)-thioridazine-2-sulfoxide. It was manufactured by Novartis.

C. Piperazine side chain:

Trifluoperazine:

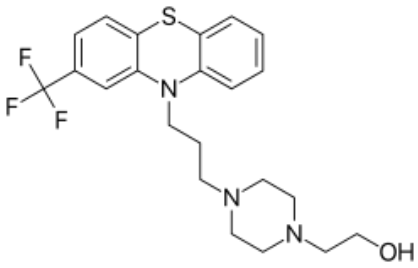


Systematic (IUPAC) name
• 10-[3-(4-methylpiperazin-1-yl)propyl]-2-(trifluoromethyl)-10*H*-phenothiazine

Trifluoperazine is an example of Phenothiazine typical antipsychotic drug. Trifluoperazine was previously widely used in the treatment of schizophrenia and psychosis. Trifluoperazine is an effective antipsychotic drug for people with schizophrenia and generalized anxiety disorder. It gives some side effects like movement problems, dry mouth, low blood pressure, nausea, and vomiting. Trifluoperazine has a central anti adrenergic, antidopaminergic, and anticholinergic effect. It works by blockading dopamine D2 and D1 receptors. It is available in the form of brand name likeEskazinyl, Eskazine, Jatroneural, Modalina, Stelazine, Terfluzine, Trifluoperaz, and Triftazin.

Fluphenazine:

Systematic (IUPAC) name
• 2-[4-[3-[2-(trifluoromethyl)-10*H*-phenothiazin-10-yl]propyl]piperazin-1-yl]ethanol

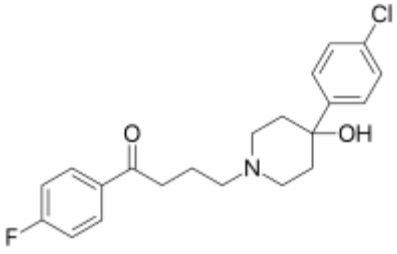


Fluphenazine is an example of Phenothiazine typical antipsychotic drug. Fluphenazinewas previously widely used in the treatment of schizophrenia and psychosis. It is available in the form of a brand name like Prolixin. It is used to treat chronic psychosis like schizophrenia. It is given by mouth, intravenous, and intramuscular injection. It gives some side effects like sleepiness, increases weight, depression, and movement problems. It may also increase prolactin level that gives milk production, enlargement of the breast, also impotence. Fluphenazine came into use in 1959.

2. Butyrophenones[10]:

Haloperidol:

Systematic (IUPAC) name
• 4-[4-(4-Chlorophenyl)-4-hydroxypiperidin-1-yl]-1-(4-fluorophenyl)butan-1-one



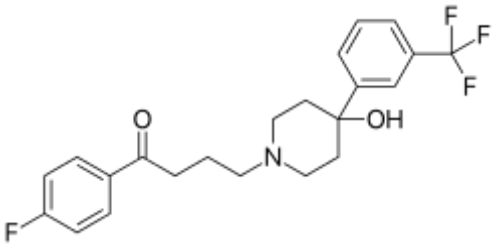
Haloperidol is an example of a typical antipsychotic drug. Haloperidol was previously widely used in the treatment of schizophrenia and psychosis. It is available in the form of a brand name like Haldol. It is also used to treat nausea, vomiting, delirium, agitation, acute psychosis, and hallucination in alcohol withdrawal. It is given by mouth, intravenous, and intramuscular injection. Haloperidol typically works within thirty to sixty minutes. Haloperidol was discovered in 1958 by the scientist Paul Janssen. It gives some side effects like Dystonia (continuous spasms and muscle contractions), Muscle rigidity, Hypotension, Constipation, Dry mouth, Blurred vision, anemia, visual disturbance, headache, Jaundice, Hepatitis, Acute hepatic failure, Liver function test abnormal Hypoglycemia, Hyperglycemia, Hyponatremia, Anaphylactic reaction, Hypersensitivity, Agranulocytosis, Neutropenia, Leukopenia, Thrombocytopenia. It gives high-affinity dopamine D_2 receptor antagonism. The drug binds preferentially to D_2 and α_1 receptors at a low dose. It gives the following effects on various receptors;

D_1 receptor	silent antagonist
D_5 receptor	silent antagonist
D_2 receptor	inverse agonist
$5HT_{1A}$ receptor	agonist
$5HT_{2C}$ receptor	silent antagonist

The bioavailability of oral haloperidol ranges from 60–70%. The drug is well and rapidly absorbed with a high bioavailability when injected intramuscularly. The bioavailability is 100% in intravenous (IV) injection, and the very rapid onset of action is seen within seconds.

Trifluperidol:

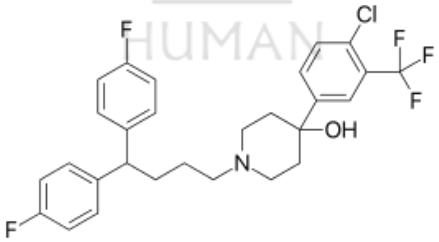
Systematic (IUPAC) name
• 1-(4-fluorophenyl)-4-[4-hydroxy-4-[3-(trifluoromethyl)phenyl]piperidin-1-yl]butan-1-one



Trifluperidol is an example of a typical antipsychotic drug. Trifluperidol was previously widely used in the treatment of schizophrenia and psychosis. It is more potent than haloperidol. It is used in the treatment of psychoses including mania and schizophrenia. . It was discovered by Janssen Pharmaceutical Company in 1959.

Penfluridol

Systematic (IUPAC) name
• 1-[4,4-bis(4-fluorophenyl)butyl]-4-[4-chloro-3-(trifluoromethyl)phenyl]piperidin-4-ol

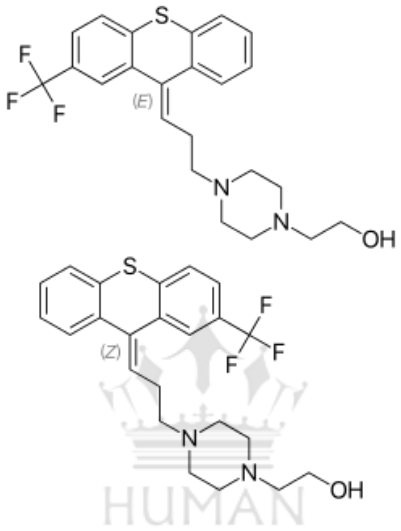


Penfluridol is an example of an anti-psychotic drug. It is a highly potent and first-generation diphenyl butyl piperidine anti-psychotic drug. Penfluridol was previously widely used in the treatment of schizophrenia and psychosis. It is available in the form of a brand name like Semap, Micefal, and Longoperidol. . It was discovered by Janssen Pharmaceutical Company in 1968.

3. Thioxanthenes[11-12]:

Flupentixol:

Systematic (IUPAC) name
• *(EZ)*-2-[4-[3-[2-(trifluoromethyl)thioxanthen-9-ylidene]propyl]piperazin-1-yl]ethanol

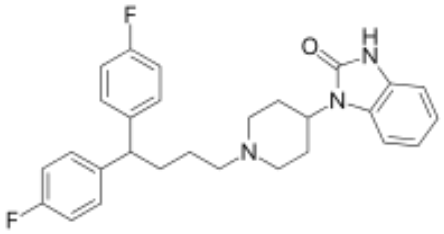


Flupentixol is also known as flupenthixol. It is available in the form of a brand name like Depixol and Fluanxol. Flupentixol is an example of a typical antipsychotic drug. It was introduced in 1965 by Lundbeck. Flupentixol is not approved for use in the United States. It was used in UK, Canada, South Africa, New Zealand and India. Flupentixoli was previously widely used in the treatment of schizophrenia and psychosis. It gives some side effects like Hypotension, Constipation, Dry mouth, Blurred vision, anemia, visual disturbance, headache, Jaundice, Hepatitis, Acute hepatic failure, Liver function test abnormal Hypoglycemia, Hyperglycemia, Hyponatremia, Anaphylactic reaction, Hypersensitivity, Agranulocytosis, Neutropenia, Leukopenia, and Thrombocytopenia.

4. Other heterocyclic:

Pimozide:

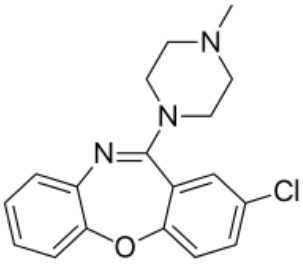
Systematic (IUPAC) name
• 1-[1-[4,4-Bis(4-fluorophenyl)butyl]-4-piperidinyl]-1,3-dihydro-2*H*-benzimidazole-2-one



Pimozide is available in the form of brand names like Orap. Pimozide is an example of an antipsychotic drug. It is highly potent and first-generation diphenyl butyl piperidine anti-psychotic drug. It was discovered by Janssen Pharmaceutical Company in 1963. It has a high potency compared to chlorpromazine. Pimozide was previously widely used in the treatment of schizophrenia and psychosis. It gives some side effects like dizziness, dry mouth, and constipation. Pimozide acts as an antagonist of the D2, D3 and D4 receptors and also 5-HT_7 receptors.

Loxapine:

Systematic (IUPAC) name
• 8-chloro-6-(4-methylpiperazin-1-yl)benzo[b][1,4]benzoxazepine

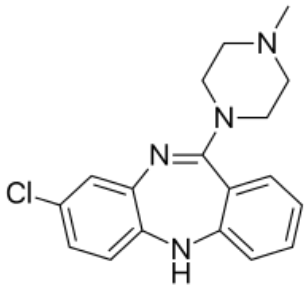


Loxapine is an example of a typical antipsychotic drug. Loxapine is highly potent drug. Loxapinewas previously widely used in the treatment of schizophrenia and psychosis disorder. It is an example of the dibenzoxazepine class of antipsychotic drug. Loxapine may be metabolized by *N*-demethylation to Amoxapine. This drug can be given by dose like 10 mg twice daily; usual dose range 30–50 mg twice daily; maximum recommended dosage is 250 mg per day. It gives common side effects like Constipation, Dry mouth, Akathisia, Dizziness, Blurred Speech, and Nasal congestion.

5. Atypical Antipsychotic[13-15]:

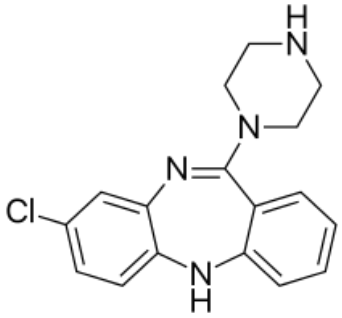
Clozapine:

Systematic (IUPAC) name
• 8-Chloro-11-(4-methylpiperazin-1-yl)-5*H*-dibenzo[*b*,*e*][1,4]diazepine



Clozapine is an example of an atypical antipsychotic drug. It is an example of the dibenzoxazepine class of antipsychotic drug. Clozapine was previously widely used in the treatment of schizophrenia and psychosis disorder. It is available in the form of brand names like Clozaril. Itis structurally related to Loxapine. It is taken by mouth. Clozapine was first made in 1958 and sold commercially in 1972. Clozapine was synthesized in 1958 by Wander AG, a Swiss pharmaceutical company. It is slightly soluble in water, soluble in acetone and highly soluble in chloroform. It binds to Serotonin and Dopamine receptors. Clozapine is an antagonist at the 5-HT_{2A} receptors/ the elimination half life of this drug is about 14 hours. Clozapine is extensively metabolized in the liver by the cytochrome enzyme. The oral bioavailability of this drug is 60 to 70% because it gives first-pass metabolism. The time to peak concentration after oral dosing is about 2.5 hours it gives major metabolite called

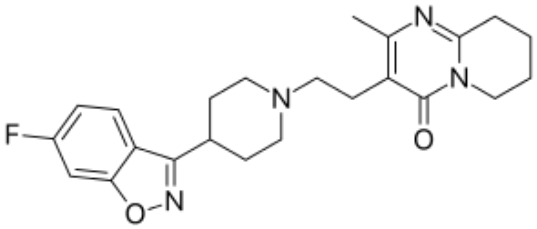
Norclozapine. It gives some side effects like dry mouth, seizures, trouble sleeping, dizziness, and drowsiness.



Norclozapine Structure (major metabolite)

Risperidone:

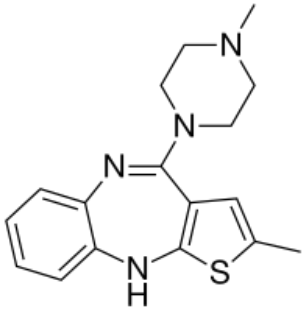
Systematic (IUPAC) name
• 3-[2-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]ethyl]-2-methyl-6,7,8,9-tetrahydropyrido[1,2-a]pyrimidin-4-one



Risperidone is an example of an atypical antipsychotic drug. It is an example of the dibenzoxazepine class of antipsychotic drugs. Risperidone was previously widely used in the treatment of schizophrenia, bipolar disorder, and psychosis disorder. It is available in the form of trade name like Risperdal. It is taken either by mouth or by intramuscular injection. It gives common side effects like movement problems, trouble seeing, constipation, and increased weight. Risperidone undergoes hepatic metabolism and renal excretion.

Olanzapine:

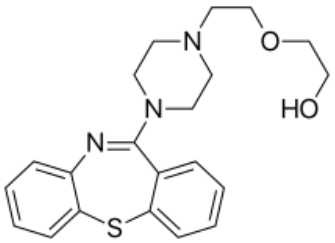
Systematic (IUPAC) name
• 2-Methyl-4-(4-methyl-1-piperazinyl)-10*H*-thieno[2,3-*b*][1,5]benzodiazepine



Olanzapine is an example of an atypical antipsychotic drug. It is an example of the thienobenzodiazepine class of anti-psychotic drugs. Olanzapine was first patented in 1971. Olanzapine was previously widely used in the treatment of schizophrenia, bipolar disorder and psychosis disorder. It is available in the form of trade names like Zyprexa. It is a newer generation of antipsychotic drug. It appears to have slightly greater effectiveness in treating schizophrenia. Olanzapine is structurally similar to Clozapine and Quetiapine. It works by blocks dopamine D2 receptors. This action is used for antipsychotics action. Olanzapine also strongly antagonizes the 5-HT_{2A} receptors. Olanzapine has a higher affinity for HT_{2A} receptors. The first-line psychiatric treatment for schizophrenia is an antipsychotic medication which includes Olanzapine. Olanzapine treatment may result in increased weight gain and increased glucose and cholesterol levels. Olanzapine is metabolized by the cytochrome P450.

Quetiapine:

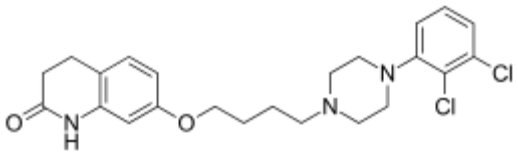
Systematic (IUPAC) name
• 2-(2-(4-Dibenzo[*b*,*f*][1,4]thiazepine-11-yl-1-piperazinyl)ethoxy)ethanol



Quetiapine is an example of an atypical antipsychotic drug. Quetiapine was previously widely used in the treatment of schizophrenia, bipolar disorder, and psychosis disorder. It is available in the form of a trading name like Seroquel. It is taken by mouth. Quetiapine was developed in 1985 and approved for medical use in the United States in 1997. Quetiapine is believed to work by blocking several receptors including serotonin and dopamine receptors. It is also used in the treatment of insomnia at low doses. It gives some side effects like Dry mouth, Dizziness, Headache, drowsiness high blood pressure, Abdominal pain, Constipation, Increased appetite, Vomiting, Increased liver enzymes, Backache, Insomnia, Tremor, Agitation, Nasal congestion, Fatigue, and Pain.

Aripiprazole:

Systematic (IUPAC) name
• 7-{4-[4-(2,3-Dichlorophenyl)piperazin-1-yl]butoxy}-3,4-dihydroquinolin-2(1*H*)-one

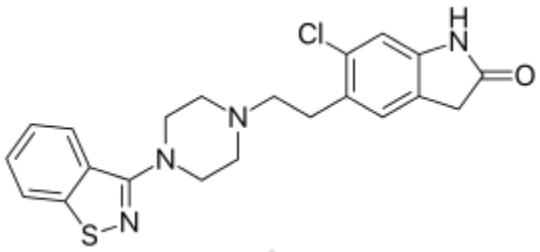


Aripiprazole is an example of an atypical antipsychotic drug. Aripiprazole is an example of phenyl Piperazine derivatives. Aripiprazole was discovered by the scientist Otsuka Pharmaceutical Company. Aripiprazole was previously widely used in the treatment of schizophrenia, bipolar disorder and psychosis disorder. It is available in the form of a brand name like Abilify. It is also used in the treatment of the major depressive disorder. It is unclear whether it is safe or effective in people less than 18 years old. Aripiprazole is effective for the treatment of acute manic episodes of bipolar disorder in adults. The

elimination half-life of this drug is approximately 75 hours. It gives 90% bioavailability when this drug is taken in the form of a tablet.

Ziprasidone:

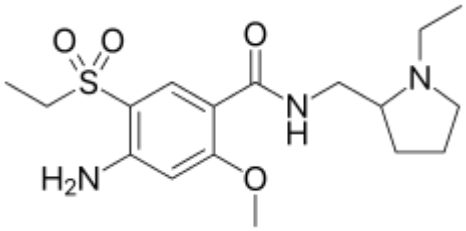
Systematic (IUPAC) name
• 5-{2-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]ethyl}-6-chloro-1,3-dihydro-2*H*-indol-2-one



Ziprasidone is an example of an atypical antipsychotic drug. Ziprasidone gained approval in the United States on February 5, 2001. Ziprasidone was previously widely used in the treatment of schizophrenia, bipolar disorder, acute mania and psychosis disorder. It is available in the form of a brand name like Geodon. Its intramuscular injection form is approved for acute agitation in people with schizophrenia. Ziprasidone is effective in the treatment of schizophrenia. Ziprasidone is a full antagonist of the D2 receptor and 5-HT_{2A}. Ziprasidone is a partial agonist for 5-HT_{1A}. Ziprasidone is similar chemically to Risperidone. Ziprasidone was first synthesized by Pfizer Pharmaceutical Company in 1987. It gives side effects like dry mouth, runny nose, respiratory disorders or coughing, nausea and vomiting, stomach aches, constipation or diarrhea, loss of appetite, weight gain.

Amisulpride:

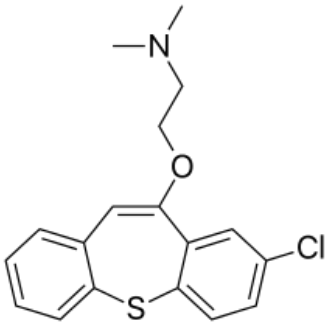
Systematic (IUPAC) name
• 4-amino-*N*-[(1-ethylpyrrolidin-2-yl)methyl]-5-ethylsulfonyl-2-methoxybenzamide



Amisulpride is an example of an atypical antipsychotic drug. It was introduced by Sanofi-Avertis in the 1990s. Amisulpridewas previously widely used in the treatment of schizophrenia, bipolar disorder, acute mania and psychosis disorder. In Italy, at a lower dosage of 50 mg per day, it is also used as a treatment for Dysthymia. It is usually classed with the newer generation of antipsychotics so that is known as atypical antipsychotic drug. It has also been found to be slightly more effective in treating schizophrenia than the typical antipsychotics. Amisulpride is believed to work by reducing dopamine D_2 receptors. It is not marketed in the Canada and US. It gives some side effects like nausea, vomiting, Anxiety, and hyperactivity. Amisulpride is antagonist for D2 and D3 dopamine receptors.

Zotepine:

Systematic (IUPAC) name
• 2-(3-chlorobenzo[b][1]benzothiepin-5-yl)oxy-*N*,*N*-dimethylethanamine



Zotepine is an example of atypical antipsychotic drug. It has been used in Germany in 1990. It was introduced by Sanofi - Avertis in 1990s. Zotepinewas previously widely used in the treatment of acute and chronic schizophrenia, bipolar disorder, acute mania and psychosis disorder. It is available in the form of brand names like Losizopilon, Lodopin, Setous, and Zoleptil. Zotepine is not approved for use in the United States, United Kingdom, Australia, Canada or New Zealand.

CONCLUSION:

Psychosis is a sign of a psychiatric disorder. Psychosis is a descriptive term for hallucination and delusion. The first-line treatment for many psychotic disorders is an anti-psychotic medication. Anti-psychotic medication like Chlorpromazine, Triflupromazine Thioridazine Trifluoperazine, Fluphenazine Haloperidol, Trifluperidol, Penfluridol, Flupenthixol, Pimozide, Loxapine, Clozapine, Risperidone, Olanzapine, Quetiapine, Aripiprazole, Ziprasidone, Amisulpride, Zotepine is used to treat a psychiatric disorder.

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