Antipsychotics: The Essentials

Module 5: A Primer on Selected Antipsychotics
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Recently approved antipsychotics
- Iloperidone (Fanapt) - 2009
- Asenapine (Saphris, Sycrest) - 2009
- Lurasidone (Latuda) - 2010

Now we’ll discuss three recently approved antipsychotics:
- Iloperidone (Fanapt) - 2009
- Asenapine (Saphris, Sycrest) - 2009
- Lurasidone (Latuda) - 2010

Iloperidone – Binding Profile
- 5HT2A/D2 antagonist
- D3 antagonist
- α1 antagonist

Iloperidone is a 5HT2A/D2 antagonist and D3 antagonist. In the case of Iloperidone, alpha 1 antagonism has direct implications regarding dose titration.
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Iloperidone – Prescribing Facts

- Dosage range:
  - 12 mg (6 mg bid) – 24 mg (12 mg bid)
- Dosage forms:
  - Tablets: 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg and 12 mg.

Weiden PJ. Clinical schizophrenia & related psychoses 2012;6:34-44.

The dosage range of Iloperidone goes from to 12 mg/ day (divided in two doses of 6 mg) to 24 mg/day (divided in two doses of 12 mg).

Iloperidone is available as tablets for oral administration of 1, 2, 4, 6, 8, 10 and 12 mg.

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Iloperidone – Clinical Profile

- Low risk of EPS (probably similar to quetiapine)
- Orthostatic hypotension can be problematic:
  - Needs slow dose titration
- Associated with greater QT prolongation than other antipsychotics.

Weiden PJ. Clinical schizophrenia & related psychoses 2012;6:34-44.

Iloperidone has a low risk (probably similar to quetiapine)

Because of its high affinity for alpha receptors, orthostatic hypotension can be problematic.

This the reason why iloperidone needs slow dose titration.

Iloperidone is associated with greater QT prolongation that other antipsychotics.
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Asenapine – Binding Profile

Asenapine is a 5HT2A/D2 antagonist that is also a partial agonist at 5HT1A receptors.

It is an antagonist at a number of serotonin receptors, including 5HT2B, 5HT2C, 5HT5A, 5HT6, 5HT7.

It also has antagonist actions at alpha 1 and histamine 1 receptors.

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Asenapine – Prescribing Facts

- Dosing range: 5-10 mg BID
- Dosage form:
  - Sublingual tablets: 5 mg, 10 mg
  - The only antipsychotic that requires sublingual administration
  - Asenapine is absorbed through the oral mucosa
  - Sublingual tablets are ineffective if swallowed
  - Eating and drinking should be avoided after asenapine administration

Asenapine is dosed between 5-10 mg BID.

Asenapine is unique in terms of formulation. The drug is available as sublingual tablets of 5 and 10 mg.

This is the only antipsychotic that requires sublingual administration.

Asenapine is absorbed through the oral mucosa.

Sublingual tablets are ineffective if swallowed

Eating and drinking should be avoided after asenapine administration
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**Asenapine – Clinical Profile**

- Approved for bipolar 1 disorder and schizophrenia
- A post hoc analysis suggests that asenapine is highly efficacious in mitigating depressive symptoms in acutely manic patients
- Associated with sedation and EPS in some patients

McIntyre RS, Wong R. Clinical schizophrenia & related psychoses 2012;5:217

I’ve highlighted some relevant clinical information from the paper by McIntyre.

Asenapine is approved for bipolar 1 disorder and schizophrenia

A post hoc analysis suggests that asenapine is highly efficacious in mitigating depressive symptoms in acutely manic patients

Asenapine is associated with sedation and EPS in some patients

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**Asenapine – Clinical Profile**

- Can result in unpleasant taste and/or oral hypoesthesia in approximately 5% of treated subjects
- A black cherry formulation is available in the US as an alternative

McIntyre RS, Wong R. Clinical schizophrenia & related psychoses 2012;5:217

The use of asenapine can result in unpleasant taste and/or oral hypoesthesia in approximately 5% of treated subjects

A black cherry formulation is available in the US as an alternative.
Lurasidone is the last antipsychotic in our list. As other second generation drugs, it’s a 5HT2A/D2 antagonist. It is a partial agonist at 5HT1A receptors. Its antagonist actions at 5HT7 and alpha2c receptors have been linked to symptom improvement in animal models of cognitive impairment.

Lurasidone is dosed in the range of 40 – 80 mg/day.

It is available as tablets of 40 and 80 mg.

It does not require initial dose titration and

Should be given with food that provides 350 cal to improve medication absorption.
Preclinical data from animal models suggests 5HT7 antagonism might play a role in cognition.

Somnolence, akathisia, parkinsonism, nausea and agitation were the most commonly reported adverse reactions.

Somnolence and akathisia appear dose related.

Considered to be weight neutral, does not have significant effects on serum lipids or glucose.

Associated with increased prolactin, which appears to be greater in females and is dose dependent.
References and Further Reading for Module 5

General Psychopharmacology Textbooks

- Tasman, A; Lieberman, J; Key, J; Maj, M. Psychiatry. 3rd ed. John Wiley & Sons, 2008

Clozapine

- Hennen J, Baldessarini RJ. Suicidal risk during treatment with clozapine: a meta-analysis. Schizophrenia research 2005
- Conley RR, Buchanan RW. Evaluation of treatment-resistant schizophrenia. Schizophr Bull 1997

First Generation Antipsychotics

- Owens D. Meet the relatives: a reintroduction to the clinical pharmacology of ‘typical’ antipsychotics (Part 1). Advances in Psychiatric Treatment 2012
- Owens D. Meet the relatives: a reintroduction to the clinical pharmacology of ‘typical’ antipsychotics (Part 2). Advances in Psychiatric Treatment 2012

New Antipsychotics