Prescribing in First Episode Psychosis

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What is special about clients with FEP?

- Antipsychotic naïve clients more sensitive to the pharmacological effects of medication[1,2,3]
  - more frequent side-effects, eg EPSE, weight gain
  - often need lower doses

- Dopamine receptor super-sensitivity
  - prolonged prescription of potent dopamine antagonist antipsychotics can induce changes in dopamine receptors leading to super-sensitivity
  - can diminish the effectiveness of antipsychotic medication over time, increase EPSE (TD) and reduce chance of being well & medication free at 7 years

- Naïvety + supersensitivity = Less D2 blockade required
  - Start low + go slow

- Cardio metabolic syndrome
  - Partial agonists vs (potent) antagonists

Need for evidence-based guidance

- Medication experiences at the beginning of treatment can have a lasting impact on future attitudes towards medication, compliance and outcomes[1]
  - critical time to optimise medical treatments
  - maximise the chance of a positive outcome for the patient
  - better efficacy, tolerability and compliance
  - positive interactions and engagement with mental health professionals[2,3,4,5]

- Medication choice is complex and evidence-based information is essential to assist prescribers in medicine optimisation

  Initial presentation

  Which first-line medication, at what dose, for how long, when to switch if there is no response, which second AP , how long, role of LAI, is it ever appropriate to combine psychotropic medications?

  Maintenance of remission

  Which antipsychotic medication is recommended for the maintenance of remission, duration of treatment, dose, etc

  Treatment resistance

  When should Clozapine be considered, dose , duration, what is Clozapine does not work?

Audit

Audit standards

- NICE guidelines

  NICE guidelines. Psychosis and schizophrenia in adults: prevention and management. Clinical guideline [CG178] Published date: February 2014. Last updated: March 2014. Available at: https://www.nice.org.uk/guidance/cg178/chapter/1-recommendations

- Maudsley guidelines

  Taylor, D, Paton C & Kapur S. 2015. The Maudsley: Prescribing guidelines in psychiatry. 12th Ed

- Recent guidelines produced by South London & Maudsley NHS Trust

  Psychosis Clinical Academic Group: Early Intervention Pathway: Practical Prescribing Issues. January 2016. South London and Maudsley NHS Trust

Audit Criteria	% compliance
The patient should be involved in the choice of antipsychotic	40
Treatment of FEP to be commenced by a specialist in secondary care	87
A second generation antipsychotic used as first line treatment	96
Antipsychotic medication trialled at optimum dosage for 4-6 weeks	13
Medication reviewed and documented in the notes, including side effects	84
Clozapine to be offered if no response following 2 different antipsychotic drugs	25

Audit

- No Trust-wide guidelines for prescribing for patients experiencing FEP
  - Prescribing practice can vary greatly
- Bath and North East Somerset (BaNES) locality working group
  - Protocol and recommendations

New Trust-wide Prescribing Protocol

NHS
Avon and Wiltshire
Mental Health Partnership
NHS Trust

Medicines Guideline: Prescribing Protocol for First Episode Psychosis (MG17)

Document authors	Assured by	Review cycle
Elena Ely - Senior Practitioner/NMP Dr Richard Stanton Dr Liz Ewins Dr Lise Paklet	Medicines Optimisation Group (MOG)	Review every two years or sooner if guidance changes. Next review

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Reviewed by / comments from:	Trust Medical Advisory Group Sarah Jones (Lead Clinical Pharmacist, East) Trust Non-Medical Prescribing Network Dr Prabhakaran Naveen (Consultant Psychiatrist, Sycamore Ward)

This guidance should be read in conjunction with the following Trust documents:
AWP Medicines Policy – P060
AWP Procedure for the prescribing, administration and monitoring of clozapine (Med20)
Guidance for Monitoring Psychotropic medications (MG11)
Interactions between tobacco smoke and medication (MG10)
Procedure for the prescription of medicines (Med02)

Population

What's so special about patients with FEP?
Neuroleptic naivety - > sensitivity
<D2 blockade required?
High response rate
High rates of substance use/misuse
Adherence is more problematic
(Buchanan *et al,* 2010; Lieberman *et al*, 2013)

Why treat people with FEP in a specialised manner?

With sustained assertive treatment over 85% of people in first episode achieve remission of symptoms within 6 months. Full remission takes time, but will occur in the majority of patients.
Overall, around 60% of patients will respond by 12 weeks and another 25% will respond more slowly.
(Murray *et al*, 2016)

Critical period (first 2-3 years)

Long term 'treatment resistant' symptoms develop during the 'critical period' so assertive treatment required.
Studies of psychosis show that long term, persisting, troublesome symptoms develop within the 'critical period' (Mason *et al*, 1995; Harrow *et al*, 1995).
There is now a growing recognition that the treatment approach required for a young person with a newly diagnosed psychotic illness, is in many ways quite different to the approach which may suit a person with more long-standing illness. Studies have identified younger, treatment naïve, patients with FEP as a population highly vulnerable to adverse metabolic 'derangements' from second generation antipsychotics (Pramyothin & Khaodhiar, 2010; Correll, 2011).

Antipsychotic free initial assessment (up to 7 Days) with baseline investigations.
If possible delay antipsychotic medication for at least two days until the diagnosis of psychosis is confirmed and organic causes are excluded.
Benzodiazepines (e.g. diazepam 10 to 30mg daily for agitation) can be used for sedation and behavioural control during this period and beyond this time as required (Taylor *et al,* 2016).

After 7 days

Choose antipsychotics following discussion of benefits and side effect profile with patient and family where possible. If patient is an inpatient or with Intensive Service discuss prescribing decision with prescriber in EI Team prior to initiating antipsychotic.
Choose a second generation antipsychotic with low side effect profile (NICE CG155 and CG178)

Start with low dose and increase slowly:
Aripiprazole 5mg 0D increasing to 10mg OD
Olanzapine 2.5 mg nocte increasing to 10mg nocte
Quetiapine 50mg daily increasing to 300mg daily
Risperidone 0.5mg daily increasing to 2mg OD
Amisulpride 25mg BD increasing to 200mg BD
(Davis *et* al, 2004; Leucht *et* al, 2013; Taylor *et al,* 2016; Murray *et al,* 2016; Zhang *et al,* 2013)

Disturbed behaviour

Try to avoid use of antipsychotics.
Use Benzodiazepines e.g. Lorazepam 1-2 mg oral.
(Taylor *et al,* 2016).

If rapid tranquilisation is needed refer to Trust Guidelines for rapid tranquilisation.
If patient is antipsychotic naïve use Lorazepam 1-2mg
(AWP Rapid Tranquillisation Procedure, Med 23).

Assess response after 2-3 weeks

- Sooner if the patient is experiencing adverse effects
- If no response after 2-3 weeks choose alternative antipsychotic with patient involved in choice (Kinon *et al*, 2010); if some response continue
- Provide information and practical help to promote and monitor concordance (Murray *et al,* 2016; Taylor *et* al, 2016; NICE CG155 and CG178)

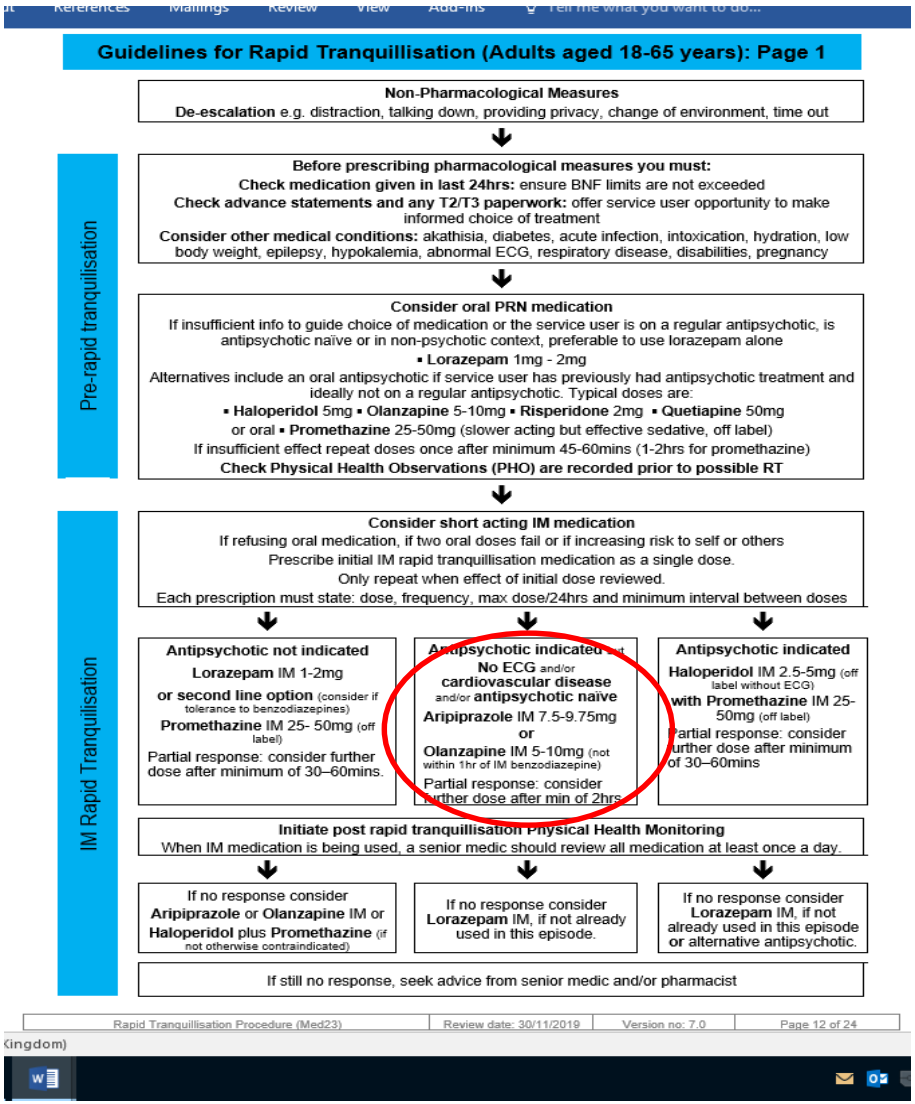
Re-assess after further 2-3 weeks

- Continue with effective dose; slowly increase/adjust depending on individual response
- Following inadequate response to two antipsychotics consider Clozapine
- Ensure patient is receiving NICE psychosocial interventions alongside medication eg CBTp, Family Interventions
- Ensure physical health checks continue as per guidelines
- Combinations of antipsychotics should not be prescribed (Buchanan *et al* 2010; Essock *et al,* 2011; Murray *et* al, 2016; Taylor *et al*, 2016; NICE CG155 and CG178)

When to cease medication

- Please consider on a case by case basis with advice from an EI prescriber
- After single episode review pros and cons of stopping at 18 months (slowly taper over at least 3 weeks)
- Multiple episodes – advise continued treatment
- Ensure appropriate monitoring in place
- Discuss use of depot when appropriate (Taylor *et al*, 2016)

Rapid Tranquilisation Policy Updated



References Mailings Review View Add-Ins Tell me what you want to do...

Guidelines for Rapid Tranquillisation (Adults aged 18-65 years): Page 1

Non-Pharmacological Measures
De-escalation e.g. distraction, talking down, providing privacy, change of environment, time out

Pre-rapid tranquilisation

Before prescribing pharmacological measures you must:
Check medication given in last 24hrs: ensure BNF limits are not exceeded
Check advance statements and any T2/T3 paperwork: offer service user opportunity to make informed choice of treatment
Consider other medical conditions: akathisia, diabetes, acute infection, intoxication, hydration, low body weight, epilepsy, hypokalemia, abnormal ECG, respiratory disease, disabilities, pregnancy

Consider oral PRN medication
If insufficient info to guide choice of medication or the service user is on a regular antipsychotic, is antipsychotic naïve or in non-psychotic context, preferable to use lorazepam alone
▪ **Lorazepam** 1mg - 2mg
Alternatives include an oral antipsychotic if service user has previously had antipsychotic treatment and ideally not on a regular antipsychotic. Typical doses are:
▪ **Haloperidol** 5mg ▪ **Olanzapine** 5-10mg ▪ **Risperidone** 2mg ▪ **Quetiapine** 50mg
or oral ▪ **Promethazine** 25-50mg (slower acting but effective sedative, off label)
If insufficient effect repeat doses once after minimum 45-60mins (1-2hrs for promethazine)
Check Physical Health Observations (PHO) are recorded prior to possible RT

IM Rapid Tranquilisation

Consider short acting IM medication
If refusing oral medication, if two oral doses fail or if increasing risk to self or others
Prescribe initial IM rapid tranquillisation medication as a single dose.
Only repeat when effect of initial dose reviewed.
Each prescription must state: dose, frequency, max dose/24hrs and minimum interval between doses

Antipsychotic not indicated
Lorazepam IM 1-2mg
or second line option (consider if tolerance to benzodiazepines)
Promethazine IM 25- 50mg (off label)
Partial response: consider further dose after minimum of 30–60mins.

Antipsychotic indicated
No ECG and/or **cardiovascular disease** and/or **antipsychotic naïve**
Aripiprazole IM 7.5-9.75mg
or
Olanzapine IM 5-10mg (not within 1hr of IM benzodiazepine)
Partial response: consider further dose after min of 2hrs

Antipsychotic indicated
Haloperidol IM 2.5-5mg (off label without ECG)
with Promethazine IM 25-50mg (off label)
Partial response: consider further dose after minimum of 30–60mins

Initiate post rapid tranquillisation Physical Health Monitoring
When IM medication is being used, a senior medic should review all medication at least once a day.

If no response consider **Aripiprazole** or **Olanzapine** IM or **Haloperidol** plus **Promethazine** (if not otherwise contraindicated)

If no response consider **Lorazepam** IM, if not already used in this episode.

If no response consider **Lorazepam** IM, if not already used in this episode **or** alternative antipsychotic.

If still no response, seek advice from senior medic and/or pharmacist

Rapid Tranquillisation Procedure (Med23) | Review date: 30/11/2019 | Version no: 7.0 | Page 12 of 24

Kingdom)

Next steps

- Guidance MG 17 now fully operational across the Trust

-> Plan to re-audit in 6 months

References

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