East London
NHS Foundation Trust

Guidelines for the Use of Melperone

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Consultation Groups	Medicines Committee and Senior Pharmacists
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Services	Applicable
Trustwide	
Mental Health and LD	
Community Health Services	

Version Control Summary

Version	Date	Author	Comment
1.0	January 2008	Prof. F. Rohricht & Seema Gadhia	Final
2.0	July 2011	Reviewed by Charity Okoli	Updated with addition of appendix containing the Melperone initiation form, Pharmacy contact details, Patient Information Leaflet for Melperone
3.0	July 2016	Reviewed by Charity Okoli	Changed the Melperone Repeat prescription. Added link to access Patient information leaflet for Melperone and link for Unlicensed Medicines policy. BPRS/Scoring sheet added as appendix. Address for Pharmacy Luton and Bedfordshire added
4.0	July 2021	Reviewed by Prof Rohricht Veena Shivath, Clinical Lead Pharmacist	6.3 BPRS forms to be uploaded onto Rio and removal of the completed melperone form to be sent to pharmacy.

Contents

Guidelines For The Use Of Melperone

About Melperone (see references for more information)

Melperone is a butyrophenone-antipsychotic with a low tendency to cause extrapyramidal side effects. It shows weak affinity for the dopamine receptors and its main antipsychotic properties seem to result from its higher 5-HT2A receptor affinity, hence described in the literature as an atypical antipsychotic. It is unlicensed in the UK and it is used in management of schizophrenia in Germany.

1.0 Introduction

1.1 This guideline is intended to ensure that melperone is used safely and monitored in accordance with the recommendations

1.2 Melperone must be initiated by Consultants only and the subsequent prescriptions can be written by either the consultant or his/her deputy delegated to provide cover in their absence.

2.0 Consent

2.1 This drug is not licensed in the UK and the patient's consent for use of an unlicensed drug must be sought and clearly documented in their medical notes. For the policy for the 'Use of unlicensed Medicines' click here

3.0 Indication

3.1 Melperone can be considered for patients with a diagnosis of treatment-refractory schizophrenia that have not responded to or cannot tolerate Clozapine.

4.0 Dosing

4.1 Melperone can be started at 25mg at night and then increased gradually according to tolerability. In non-refractory illness, doses of 100-300mg a day are effective. Higher doses may be needed in refractory illness. The maximum licensed dose is 600mg/day.

4.2 The daily dose must be given in divided doses, with a higher evening dose being selected (at least during initiation phase) in order to achieve a more pronounced sedative effect. It is best taken after meals and before bedtime.

5.0 Baseline physical observations

5.1 Before starting Melperone, it is advisable to have the following tests; a full blood count, an ECG and blood pressure must be monitored.

5.2 A baseline BPRS is also required before treatment is started which will have to be uploaded onto Rio notes.

6.0 Prescribing of Melperone

6.1 Melperone must be used alone and not in conjunction with another antipsychotic. However, whilst switching from another antipsychotic to melperone a cross over period may be necessary and as soon as a therapeutic dose of the melperone is reached, the other antipsychotic must be discontinued.

6.2 For every patient prescribed Melperone, a “Melperone initiation form” must be completed to allow monitoring and audit of the patients. The completed form must be sent to the pharmacy department to allow dispensing and a copy uploaded onto Rio. Local arrangements must be made for supply of the melperone and collection by patients as this medication will be issued by the pharmacy department during treatment. GPs must subsequently be informed about this treatment and necessary monitoring.

6.3 A copy of the baseline BPRS must be uploaded onto Rio together with the melperone prescription. Subsequent BPRS must be carried out at 6 weeks, 3 months, 6 months and during each review of the patient. All completed BPRS paperwork must be uploaded onto Rio.

6.4 On discharge, the prescribing of melperone must not be transferred to primary care but the GP must be informed about the new medication to be added to the summary care records (SCR). Prescribing should be continued by secondary care and the prescription must be reviewed every six months.

6.5 Request for repeat prescriptions should be made by using the using the Melperone repeat prescription
(Appendix B). The completed repeat prescription should be forwarded to pharmacy department (see
Appendix C) for pharmacy contact details.

6.6 Melperone should not be prescribed on FP10 prescription pad.

6.7 All data relating to patients prescribed melperone in this Trust will be reviewed after 12 months.

6.8. Melperone has been identified as being a CYP inhibitor and caution should be exercised when used with drugs known to act as CYP inhibitors (see Hefner et al 2020); if used as co-medication for augmentation purposes of another antipsychotic the potential impact re an increase of higher plasma concentrations must be considered.

6.9. Melperone can be considered for treating psychosis in patients with known epilepsy; there is some limited evidence for a beneficial effect on reducing seizure frequency (Gorska et al, 2019) .
6.10. A multicentre DBPCT demonstrated that melperone was not effective in the treatment of Parkinson Disease in psychosis. But - similar to clozapine and quetiapine – Melperone did not worsen motor function in PD patients (Freidman, 2012).

6.11. In a recently published guideline paper Melperone was identified as having a moderate effect (>10 ms) to cause a QT prolongation at clinical doses (similar to Amisulpride, Chlorpromazine, Levomepromazine, Iloperidone, Quetiapine, Ziprasidone); therefore ECG monitoring guidelines are the same as for the other antipsychotics listed here (see Lambiase et al., 2019).

7.0 For the Melperone Patient Information Leaflet click here

8.1 Appendix A

East London NHS
NHS Foundation Trust

Medicines Committee

Melperone initiation form

This form must be completed in full for all patients being initiated on melperone.

Patient name……. **Age ……**

Gender **M/F**

Diagnosis (choose one)
Refractory Schizophrenia
Schizophrenia
Schizoaffective disorder
Bipolar affective disorder

Other (state) ……..……

Race (choose one)
White
Black African
Black Caribbean
Asian

Other (state) ……..……

Duration of illness ..……years **……months**
(i.e. time since first diagnosis of above)

Duration of current stay……days

Prescribed antipsychotic(s) immediately before melperone (state)……..……..

History of prior clozapine prescription **Y/N**

Reason for starting melperone (choose one)

Intolerance to clozapine:
- **Neutropenia**
- **Other (state)……..**

Ineffectiveness of prior treatment

Other (state) ……..

Starting dose of melperone: ……

List all other drugs currently co-prescribed
(dosing details not required; include PRN but state which)

1.
2.
3.
4.
5.

Physical Healthcare Baseline Observations:

ECG	**Y / N**
Blood pressure	**_____ / _____**
FBC	**Y / N**

	Date	**Score**
Baseline BPRS Score		
6/52 BPRS Score		
3/12 BPRS Score		
6/12 BPRS Score		

Prescriber's name ……..

Consultant ……..

Directorate/borough……..

8.2 Appendix B

Rating Scales for Psychosis

Brief Psychiatric Rating Scale (BPRS)

What is it ?
The BPRS is probably the most widely used rating scale to assess the clinical outcome of schizophrenia. It is a 24-item scale (sometimes 18 or 20) that quantifies psychosis, depression and anxiety symptoms.

The use of this scale enables health care professionals to quantify and monitor severity of symptoms, especially in response to antipsychotic medication.

Who are the raters ?
Raters can be psychiatrists, nurses, psychologists or other trained health care professionals.

How long does it take?
Between 15 to 30 minutes.

How is it used?
Each item is rated by giving it a score between 1 and 7 (1 = not present, 7 = extremely severe). The items are described in detail over leaf.

It is worth noting that a score of 24 is normal.

How often should it be done ?
Ideally, BPRS should be done ***before*** starting antipsychotic treatment and then every week. A response should be seen after 6 weeks. Where a drug is being used to augment existing treatment, BPRS should be rated before the second drug is added.

What is defined as a response?
Most clinical trials evaluating the efficacy of antipsychotic medication define a response as a 20% reduction in BPRS score, although a clinically relevant improvement may only be reflected in a 30% or more decrease.

Brief Psychiatric Rating Scale (BPRS)

Please enter the score which best describes the patient's condition.
0 = not assessed, 1 = not present, 2 = very mild, 4 = moderate, 5 = moderately severe, 6 = severe, 7 = extremely severe

1.	**SOMATIC CONCERN:** Degree of concern over present bodily health. Rate the degree to which physical health is perceived as a problem by the patient, whether complaints have a realistic basis or not.	Score ☐
2.	**ANXIETY:** Worry, fear, or over concern for present or future. Rate solely on the basis of verbal report by patient, not observed anxiety which is rated under Tension.	Score ☐
3.	**DEPRESSION:** Includes sadness, unhappiness, anhedonia and preoccupation with depressing topics (can't attend to TV or conversations due to depression), hopelessness, loss of self-esteem. Do not include vegetative symptoms, e.g motor retardation, early waking or the amotivation that accompanies the deficit syndrome.	Score ☐
4.	**SUICIDALITY:** Expressed desire, intent or actions to harm or kill self.	Score ☐
5.	**GUILT:** Over concern or remorse for past behaviour. Rate only patient's statements, do not infer feelings from depression, anxiety or neurotic defenses.	Score ☐
6.	**HOSTILITY:** Animosity, contempt, belligerance, threats, arguments, tantrums, property destruction, fights and any other reports of hostile attitudes or actions. Rate solely on the basis of the verbal report of feelings and actions of the patient toward others. Do not infer hostility from neurotic defenses, anxiety or somatic complaints. Do not include incidents of appropriate anger or obvious self-defence.	Score ☐
7.	**ELEVATED MOOD:** A pervasive, sustained and exaggerated feeling of well-being, cheerfulness, euphoria (implying a pathological mood), optimism that is out of proportion to the circumstances. Do not infer elation from increased activity or from grandiose statements alone.	Score ☐
8.	**GRANDIOSITY:** Exaggerated self-opinion, conviction of special abilities or powers or identity as someone rich or famous. Rate only patient's statements about himself, not his demeanour.	Score ☐
9.	**SUSPICIOUSNESS:** Expressed or apparent belief that others have now, or have had in the past acted with a malicious or discriminatory intent. Include persecution by supernatural or other non-human agencies (e.g the devil).	Score ☐
10.	**HALLUCINATIONS:** Perceptions without normal external stimulus. Rate only those experiences which are reported to have occurred in the last week and which are described as distinctly different from the thought and imagery processes of normal people.	Score ☐
11.	**UNUSUAL THOUGHT CONTENT:** Unusual, odd, strange or bizarre thought content. Rate the degree of unusualness, not the degree of disorganisation of speech. Include thought insertion, withdrawal and broadcast. Include grandiose, somatic and persecutory delusions even if rated elsewhere.	Score ☐
12.	**BIZARRE BEHAVIOUR:** Reports of behaviours which are odd, unusual or psychotically criminal. Not limited to interview period. Include inappropriate sexual behaviour and inappropriate affect.	Score ☐
13.	**SELF-NEGELCT:** Hygiene, appearance or eating behaviour below usual expectations, below socially acceptable standards or life threatening.	Score ☐
14.	**DISORIENTATION:** Does not comprehend situations or communications such as questions asked during the entire interview. Confusion regarding person, place or time. Do not rate if incorrect responses are due to delusions.	Score ☐
15.	**CONCEPTUAL DISORGANISATION:** Degree to which speech is confused, disconnected, vague or disorganised. Rate on the basis of integration of the verbal products of the patient. Do not rate on content of speech.	Score ☐

Brief Psychiatric Rating Scale (BPRS)

Please enter the score which best describes the patient's condition.
0 = not assessed, 1 = not present, 2 = very mild, 4 = moderate, 5 = moderately severe, 6 = severe, 7 = extremely severe

16.	**BLUNTED AFFECT:** Restricted range in emotional expressiveness of face, voice and gestures. Marked indifference or flatness even when discussing distressing topics.	Score ☐
17.	**EMOTIONAL WITHDRAWAL:** Deficiency in patient's ability to relate emotionally during interview situation. Use your own feeling as to the presence of an "invisible barrier" between patient and interviewer. Include withdrawal apparently due to psychotic processes.	Score ☐
18.	**MOTOR RETARDATION:** Reduction in energy level evidenced by slowed movements and speech, decreased number of spontaneous body movements. Rate on basis of observed behaviour of the patient only. Do not rate on the basis of patient's subjective impression of his own energy level. Rate regardless of medication effects.	Score ☐
19.	**TENSION:** Physical and motor manifestations of tension "nervousness" and agitation. Self-reported experiences of tension should be rated under the item on anxiety. Do not rate if restlessness is solely akathisia, but do rate if akathisia is exacerbated by tension.	Score ☐
20.	**UNCOOPERATIVENESS:** Resistance and lack of willingness to cooperate with interview. The uncooperativeness might result from suspiciousness. Rate only uncooperativeness in relation to the interview, not behaviours involving peers and relatives.	Score ☐
21.	**EXCITEMENT:** Heightened emotional tone or increased emotional reactivity to interviewer or topics being discussed, as evidenced by increased intensity of facial expressions, voice tone, expressive gestures or increase in speech quantity and speed.	Score ☐
22.	**DISTRACTIBILITY:** Degree to which observed sequences of speech and actions are interrupted by stimuli unrelated to the interview. Distractibility is rated when the patient shows a change in the focus of attention as characterised by a pause in speech or a marked shift in gaze. Rate even if the distracting stimulus cannot be identified.	Score ☐
23.	**MOTOR HYPERACTIVITY:** Increase in energy level evidenced in more frequent movement and / or rapid speech. Do not rate if restlessness is due to akathisia.	Score ☐
24.	**MANNERISMS AND POSTURING:** Unusual and bizarre behaviour, stylised movement or acts, or any postures which are clearly uncomfortable or inappropriate. Exclude obvious manifestations of medication side effects. Do not include nervous mannerisms that are not odd or unusual.	Score ☐
	TOTAL	**Score** ☐

Patient name:

Rater:

Date of assessment:

Date of next BPRS:

Brief Psychiatric Rating Scale (BPRS)

Score sheet

Name of patient:

Date of assessment	Rater	Antipsychotic medication / dose	BPRS score

8.3 Appendix C
Please return the form to Pharmacy

Melperone Repeat prescription

Patient Details			
First Name		Surname	RIO no:
D.o.b:	Unit/Team: Contact Number:	Consultant :	NHS no:
Care Co-ordinator: Contact number:			
Drug allergies:			
Dispensing/Collection details and any other relevant notes			
Compliance aid required: Yes/No **(*delete as appropriate)**			
Notes:			

PRESCRIPTION (Prescriptions to be reviewed every six months)

Date	Drug (approved name) and dose form	Dose	Frequency	Prescribed by sig.	Screened by (pharmacy)

DISPENSING RECORD (Prescriptions are dispensed as outpatients)

QUANTITY	D	C	QUANTITY	D	C
1.			**3.**		
	Date	Date		Date	Date
2.			**4.**		
	Date	Date		Date	Date

8.4 Appendix D:Pharmacy Contact Details

8.4.1 Pharmacy Department
Newham Centre for Mental Health
Cherry tree Way
Glen Road
Plaistow, London
Tel: 02075404380 Ext: 2130, 2065 OR bleep pharmacist via Switch board
Fax: 02075404200

8.4.2 Pharmacy department
Mile End Hospital
Bancroft Road
London
E1 4DG
Email: elft.pharmacytowerhamlets@nhs.net

8.4.3 Pharmacy department
City & Hackney
East Wing
Homerton Hospital
Homerton Row
London
E9 6SR
Tel: 02085108174/7250
Fax: 02085107251
Email: elft.pharmacycityandhackney@nhs.net

8.4.4 Pharmacy department
Luton & Central Bedford
Mental Health Unit
LU4 0FB
Email: elft.pharmacyluton@nhs.net

References:

1. Bobo, W V; Jayathilake, K; Lee, M A; Meltzer, H Y (July 2009). "Melperone, an atypical antipsychotic drug with clozapine-like effect on plasma prolactin: contrast with typical neuroleptics". Human Psychopharmacology: Clinical and Experimental. **24** (5): 415–422.

2. Gahr, M; Gastl, R; Kölle, M A; Schönfeldt-Lecuona, C; Freudenmann, R W (2012). "Successful treatment of schizophrenia with melperone augmentation in a patient with phenotypic CYP2D6 ultrarapid metabolization: a case report". Journal of Medical Case Reports. **6** (1): 49.

3. Röhricht, F; Gadhia, S; Alam, R; Willis, M (2012). "Auditing Clinical Outcomes after Introducing Off-Licence Prescribing of Atypical Antipsychotic Melperone for Patients with Treatment Refractory Schizophrenia" The Scientific World Journal. **2012**:
4. Whiskey, E; Vavrova, M; Gaughran, F; Taylor, D (February 2011). "Melperone in Treatment-Refractory Schizophrenia: A Case Series". Therapeutic Advances in Psychopharmacology. **1** (1): 19–23.
5. Note: Prescribers can also request for a copy of Melperone data sheet available from pharmacy office, Newham Centre for Mental Health.
6. Gudrun Hefner et al. Prevalence and sort pf pharmacokinetic drug-drug interactions in Hospitalised psychiatric patients. Psychiatry and Preclinical Psychiatric Studies; Journal of Neural Transmission, vol 127, 1185-1198.