19 - Chapter 14 Prescribing psychotropics

01 - Working towards adherence

Working towards adherence

02 - What is adherence

What is adherence?

03 - How common is non adherence

How common is non-adherence?

The Maudsley® Prescribing Guidelines in Psychiatry, Fifteenth Edition. David M. Taylor, Thomas R. E. Barnes and Allan H. Young. © 2025 David M. Taylor. Published 2025 by John Wiley & Sons Ltd. Chapter 14 Working towards adherence What is adherence? The first clear statement about adherence comes from Hippocrates (460–377 bc), who vividly described non-adherence and linked it with poor outcomes. The World Health Organization (WHO) has described adherence as ‘the extent to which a person’s behaviour – taking medication, following a diet, and/or executing lifestyle changes – corresponds with agreed recommendations from a healthcare provider’.1 In the UK, the National Institute for Health and Care Excellence (NICE) has, more succinctly, defined adherence as ‘the extent to which the patient’s action matches the agreed recommendations’.2 The more traditional notion of the patient ‘complying’ with the doctor’s orders seems patronising and to deny the agency of the patient.3 ‘Concordance’ is another term that has been used, which seems to refer to an agreement between the patient and the doctor. This is part of the notion of informed consent and is essential for a ‘prescribing partnership’ with patients.4 But, as we know, agreement about a course of action does not necessarily guarantee that the action will happen. Thus ‘adherence’ will be used in this section to refer to the development of behaviours that will, it is hoped, result in better outcomes for our patients. How common is non-adherence? Large numbers of people, in most areas of medicine, do not seem to take their tablets very regularly – and so can be said to be partly or fully non-adherent. This is a phenomenon that arises in other clinical areas as well, such as psychological therapies. For people referred to psychotherapy services in the north of England, 34% did not attend for their first assessment session and, of those who did, only 57% subsequently attended the first treatment session.5 Prescribing psychotropics

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Impact of non-adherence

928 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 14 For chronic physical and mental disorders, the picture is not much better. Although 76% of patients with several conditions reported adhering to medication, electronic monitoring suggested that, in fact, only 44% did so.6 Consistent with previous findings, a 2020 meta-analysis suggested that, overall, about 50% of people with mental health problems do not take their medication as prescribed.7 This, however, may be an oversimplification. It is probable that a small proportion of patients are fully adherent, the majority are partially adherent to varying degrees, and a few never take any medication at all (of their own volition).8 These findings are not only characteristic of western medical culture, they are reflected in other parts of the world.9 Adherence rates also vary both over time and across settings. For example, 10 days after discharge from hospital, up to 25% of patients with schizophrenia are partially or completely non-adherent with oral treatment and this figure rises to 50% at 1 year and to 75% by 2 years.10 Other studies have reported 25.8% complete discontinuation of medication within 1 year of discharge from hospital.11 In some mental healthcare settings, the rate of non-adherence may be as high as 90%.12 Diagnosis may also be significant. An Austrian study found that significantly more patients with schizophrenia (66%) did not take their medication as prescribed, compared with patients with affective disorders (47%) or those with other psychiatric diagnoses (41%).13 A major issue is that poor adherence almost always occurs without the knowledge of the prescriber. In one study, prescribers identified only half of those who were non- adherent.14 In another, 35% of patients referred for treatment of (apparently) refractory schizophrenia had sub-therapeutic plasma concentrations and many of them had plasma levels of zero.15 Impact of non-adherence Medicines are only effective if taken at a therapeutic dose. And they are effective. A 20- year follow-up study of 62 250 patients with schizophrenia reported a significantly lower suicide mortality during antipsychotic use compared with non-use.16 Antipsychotic use also decreased overall mortality. Poor adherence to medication is a major risk factor for worse outcomes including relapse in people with schizophrenia,17–19 bipolar disorder20 and depression.21 Wider health benefits are also lost. Depressed patients who do not take an antidepressant have a 20% increased risk of an incident myocardial infarction compared with those who do.22 The serious consequences of non-adherence with medication may be mitigated by implementing routine monitoring. Data were collected as part of the National Confidential Inquiry into Suicide and Homicide by People with Mental Illness.23 This revealed that healthcare providers who had a policy regarding how to manage patients who are not taking their medication as prescribed had 20% fewer suicides than providers who did not have such a policy.23

Another reason that poorly adherent individuals do worse is that they may stop their medication abruptly and without monitoring (and without telling anyone). Abrupt cessation of almost all psychotropic drugs tends to worsen prognosis (see The Maudsley Deprescribing Guidelines). One of the findings that clearly illustrate the benefits of adherence is the example of depot antipsychotic medications. They do not differ pharmacologically from their oral equivalents but have consistently been shown to result in lower rates of readmission to

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Prescribing psychotropics CHAPTER 14 hospital. The only difference is that with the depot preparations, adherence is, for a while at least, assured (and known about) – something which cannot be said for oral medications. Improving adherence offers substantial possibilities for improving the outcomes from treatments. WHO comments that ‘increasing the effectiveness of adherence interventions may have far greater impact on the health of the population than any improvements in specific medical treatments’.1 We must also remember that medication is not the only effective treatment for psychosis. Although a meta-analysis24 and systematic review25 of such psychodynamic interventions (which included studies in unmedicated patients) confirmed the superiority of treatment with antipsychotics, the most recent systematic review of psychosocial interventions for psychotic patients (with no or low-dose antipsychotics) found the effect of such interventions to be equal to treatment with antipsychotics.26 Cognitive behavioural therapy (CBT) for psychosis has been demonstrated to reduce certain symptoms, although its effect on quality of life does not seem to be significant.27 So – we certainly need better drugs, but we need also to improve adherence. Factors affecting adherence7,28 Table 14.1 lists many of the factors that might affect adherence. Clearly, not all of these factors necessarily fit into a single category. For example, poor understanding by the patient can either be due to poor health literacy and/or numeracy or can be due to deficiencies in communication by the doctor. Assessing adherence29,30 Table 14.2 outlines methods of assessing medication adherence. For some antipsychotics such as clozapine, olanzapine, aripiprazole and risperidone, blood tests can be used to directly assess plasma levels. However, the plasma levels of these drugs attained with a fixed dose do vary, as do the therapeutic effects in individuals. It is therefore not possible to accurately determine partial non-adherence. That is to say, total non-adherence will be readily revealed (plasma level = zero) but partial and full adherence may be difficult to tell apart. Table 14.1 Factors affecting adherence. Illness-related Treatment-related Clinician-related Patient-related Environmental Lack of motivation Poor insight Grandiose delusions Cognitive deficit Thought disorder Forgetfulness Disorganisation Adverse effects Dysfunctional beliefs Inappropriate medication preparation or packaging Dosing schedules31,32 Poor therapeutic alliance Lack of follow-up Limited consultation time Poor provision of information and explanation Denial Poor insight Comorbidities Physical impairments Poor literacy Poor health literacy33 Poor understanding of treatment options Disorganised environment Family’s beliefs Religious beliefs Health beliefs

930 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 14 Table 14.2 Assessing adherence. Method Variables measured Advantages Disadvantages Direct Blood test Drug/metabolite plasma levels Accurate Invasive Costly Inter-individual variations (e.g. fast and slow metabolisers) Not reliable for all drugs (see text) Only a result of zero can be definitively interpreted Information only relevant for a very limited timeframe No information about the patterns of medication-taking behaviour, levels of adherence or factors that may change adherence Indirect Pill count Number of missing tablets/ missed prescriptions Simple to use (useful in clinical trials) Labour-intensive in clinical practice Substantial evidence that pill counts underestimate levels of non-adherence Electronic database: clinical/pharmacy records History of non-adherence (but generally with very little detail or formal assessment) Pharmacy dispensing and collection records (e.g. medication possession ratio – MPR) Readily accessible Easy to identify non-adherent patients Inexpensive Non-invasive Not reliable – only provides evidence for collection and possession of medication Self-report Validated assessment scales (questionnaires) (e.g. Medication Adherence Rating Scale – MARS) Easy to use Inexpensive Subject to reporting bias Tendency to please clinicians Massively overestimates adherence Subjective Electronic monitoring devices (e.g. Medication Event Monitoring System – MEMS) Number of times medication container has been opened and (assumed) percentage of doses removed Among the most accurate methods Objective Provides additional information on medication-taking behaviour Expensive Bulky containers Not evidence for ingestion of medication – only of container opening Patient feels under surveillance

07 - Monitoring adherence and assessing attitudes

Monitoring adherence and assessing attitudes to medication

08 - Enhancing medication adherence

Enhancing medication adherence

Prescribing psychotropics CHAPTER 14 Monitoring adherence and assessing attitudes to medication Psychiatrists generally prefer to use direct questioning over the use of more intrusive/ objective and elaborate methods of assessing adherence. Partly as a result non-adherence may go undetected.34 NICE recommends that the patient should be asked in a non- judgemental way if they have missed any doses over a specific time period such as the previous week.35 Issues of forgetfulness aside, whether the patient takes medication or not will be, to a significant extent, determined by their views about medication and its perceived effect on their life and condition. Rating scales and checklists can help the clinician to guide and structure a discussion of what the patient thinks and feels about medication. The most widely used is the Drug Attitude Inventory (DAI),36 which consists of a mix of positive and negative statements about medication; 30 statements in its full form and 10 in its short form. The patient completes it by simply agreeing or disagreeing with each statement. The total score is an indicator of the patient's overall perception of the balance between the benefits and harms associated with taking medication, and therefore likely adherence. Attitudes to medication as measured in this way have been shown to be a useful predictor of adherence over time.37 Other checklists include the Rating of Medication Influences (ROMI) scale,38 the Beliefs about Medicines Questionnaire39 and the Medication Adherence Rating Scale (MARS).19 Enhancing medication adherence Adherence to medication requires collaboration between the patient and the prescriber. NICE recommends that, as long as the patient has capacity to consent, their right not to take medication should be respected. If the prescriber considers that this decision may lead to harm, the reasons for the patient's decision and the prescriber's concerns should be recorded. Adherence is a complex behaviour that is influenced by malleable underlying factors. Consequently, determinants of non-adherence can be modified through patient-specific and factor-focused interventions (Table 14.3). However, most adherence-enhancing interventions are not based on a sound theoretical framework and lack methodological rigour.40 Low-quality studies and their outcomes are often not duplicated in different settings. This phenomenon was also highlighted by the most recent Cochrane review of adherence interventions when they reported that only 11 studies out of 182 included papers had the lowest risk of bias.41 Strategies for improving adherence Systematic reviews suggest that patient-specific interventions are more likely to enhance adherence in patients with serious mental disorders.42 NICE has reviewed the

evidence for adherence over a range of health conditions and concluded that no specific intervention can be recommended for all patients. Note that few studies in this area specifically recruited non-adherent patients (the refusal rate in such patients is likely to be high) and the specific barriers to adherence are rarely identified. The small effect size seen in many studies may simply be a consequence of this unfocused approach. An intervention mapping framework43 provides a way to connect determinants of non-adherence to evidence-based interventions.

932 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 14 Medication-taking aids ‘Compliance aids’ are boxes that contain compartments that can accommodate up to four doses of multiple medicines each day. These may be helpful in patients who are clearly motivated to take medication but who are disorganised or who have cognitive deficits. But only 10% of non-adherent patients say that they simply forgot to take medication, so medication-taking aids are not a substitute for lack of insight or lack of motivation. Moreover, some medicines are unstable when removed from blister packaging and placed in a compliance aid. These include oro-dispersible formulations which are often prescribed for non-adherent patients. In addition, medication-taking aids are labour-intensive (expensive) to fill, it can be difficult to change prescriptions at short notice and the process of filling of these devices is particularly error-prone.46 More sophisticated programmes of practical support, both electronic and in-person, have been shown to be effective.47 Depot/long-acting antipsychotics Meta-analyses of clinical trials have shown that the relative and absolute risks of relapse with depot maintenance treatment were 30% and 10% lower, respectively, than with oral treatment.48,49 NICE recommends that depots are an option in patients who are known to be non-adherent to oral treatment and/or those who prefer this method of administration. However, it is worth remembering that switching a non- adherent patient from oral antipsychotics to a long-acting injectable formulation does not address the underlying reasons driving that non-adherence. This has been highlighted by a recent systematic review that reported a rate of discontinuation of above 50% in those who had been prescribed second-generation depots.50 So long-acting antipsychotics do not stop non-adherence but they do prevent sudden cessation of medication and its consequences (all depots provide a slow decline in plasma levels). Table 14.3 Interventions for non-adherence.44 Intentional non-adherence Unintentional non--adherence Psychoeducation is the foundation for all adherence interventions, but without behaviour-changing components it is not overwhelmingly effective. Provides both verbal and written information. Motivational interviewing for goal-setting Adherence therapy for exploring dysfunctional beliefs about medication or the illness, providing information and goal setting. It requires more time and multiple sessions. Cognitive behavioural therapy to eradicate or control the residual symptoms that prevent adherence. To address dysfunctional beliefs about treatment. Cognitive remediation to help with cognitive deficit in psychotic patients and thought disorder Mindfulness to help with symptoms Monitor adverse effects regularly and periodically Therapeutic alliance – a non-judgemental clinician allows patients to honestly disclose their thoughts and beliefs about medication Family intervention – psychoeducation and family therapy Simplify dose regimen – reduce number of medications and/or frequency of administration Dispensing interventions – medication-taking aids EAM (electronic adherence monitoring) – evidence for this is weak45 Pairing-up medication – taking with a daily activity (e.g. having breakfast, brushing teeth or before bedtime) Use technology – messaging service, email and telephone reminders Pharmacy interventions for those with physical impairment (e.g. opening bottles)

Prescribing psychotropics CHAPTER 14 Their use can also provide certainty about the level of adherence (the injection is either given or it is not). Depots are probably underused, for example a US study found that depot preparations were prescribed for fewer than one in five patients with a recent episode of non-adherence.51 An alternative to depots is the use of long-acting oral antipsychotics such as penfluridol, which can be given weekly.52 Supervised administration obviates the need for injections but does not provide the same level of certainty over compliance given the facility that patients have demonstrated for disguising the taking of oral medication. In the USA, Abilify MyCite is approved for use.53 This is a version of aripiprazole with a transmitting sensor embedded in the formulation which is able to confirm that a tablet has been taken. Evidence for its effectiveness is slim.54 Financial incentives Controlled trials in a number of disease areas support the offer of financial incentives to enhance medication adherence. Paying people to take their medication is extremely controversial, though some clinicians have found this strategy to be effective. The effect could not be maintained in a randomised controlled trial (RCT) at 6- and 24-month follow-up after payments were stopped, and complete adherence was achieved in only 28% of patients receiving the incentives.55 Other RCTs also have demonstrated a significant increase in adherence during the trial and a decline at follow-up when payments had stopped.56 Offering financial incentives did not reduce patients' motivation for treatment.57 A systematic review of acceptability of financial incentives for health- related behaviours has raised concerns about the validity and reliability of these interventions given their methodological limitations.58 Psychological interventions In physical medicine, medication adherence has been found to be associated with health beliefs and psychological variables, such as self-efficacy and locus of control.59 Family support is also positively related to medication adherence. It is likely to be the same in psychiatry – but what can be done? One such intervention – called, at the time, 'compliance therapy' – was evaluated at the Maudsley Hospital.60 This was a pilot of a mixed intervention, consisting of active listening, cognitive behavioural techniques, motivational interviewing and the provision of information and explanation. This showed promising results in terms of increased adherence and reduced admission rates over the next 6 months. However, training for staff and supervision render it time-consuming. A subsequent replication did not show the same improvements,61 but also did not appear to have incorporated a training or supervisory element for those delivering the therapy. However, a trial of training in compliance therapy did seem to have an effect on the junior doctors involved, who felt that they were more aware of the drivers of non-adherence and of the importance of empathic listening and more able to understand why a patient might not take medication.62 One prerequisite for successful adherence to a treatment regimen should be that the patient understands the objectives of treatment, the options on offer and the rationale behind them. However, many – perhaps most – doctors have had no specific training in how to convey information and understanding to patients. Difficulties have been noted

09 - Conclusion

Conclusion

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934 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 14 to arise in cancer medicine regarding the benefits and risks of anti-cancer medications.63 One must assume that we are likely to meet the same difficulties in psychiatry. We also need to consider that our patients may have a very different explanatory model for what is happening to them. For example, not so long ago, only just over a third of white English patients viewed schizophrenia as having a substantially biological origin.64 So our explanations for a person's psychosis may not be as convincing to them – and their families – as we might imagine. One simple step that might help is to encourage patients with a serious medical illness to read their own notes; one study reported that this helped such patients to better understand why they were prescribed medications.65 However, this begs the question of why they did not understand in the first place. The range of practical interventions described in Table 14.3 – and, to a great extent, the psychological interventions contained in the original model of compliance therapy – will need to be tailored to the needs of the individual patient. But this assumes that clinicians have an awareness of the issue, the requisite skills and the time available to use them. The current RCPsych curricula, although they refer to some of the psychological skills modalities mentioned, do not include the management of adherence as an issue in either the core curriculum or the general psychiatry curriculum.66 Conclusion Establishing and maintaining adherence is a quintessentially biopsychosocial activity. It is central to the practice of medicine and, hence, to psychiatry. It demands both an awareness of the problem, a knowledge of practical strategies for its improvement and a repertoire of psychological skills. The neglect of this area of therapeutics in training should not deter prescribers from recognising non-adherence and taking active steps to manage it. An initial gambit might be, at the end of any first prescription, to ask ourselves 'What have I done to help this patient take this medication?' and to record this answer as part of the care plan, as a reminder to ourselves and our colleagues that this issue needs our conscious, structured and regular attention. References

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Restarting psychotropic medications after a period of non-compliance

Prescribing psychotropics CHAPTER 14 Restarting psychotropic medications after a period of non--compliance When a patient is admitted to hospital it is often because they have been non--compliant with their medications for some time before admission. The clinical question of whether to restart the medication and at which dose is a complex one. The risk of withdrawal symptoms and relapse must be balanced against the risk of adverse drug reactions when medications are reintroduced too quickly. There is little published evidence on this area, with most guidance (often of undeclared provenance) coming from manufacturers. The guidance below should be followed with caution. Summaries of product characteristics (SPCs) and other formal, regulatory documents tend not to deal with the issue of restarting medication. Official patient information leaflets sometimes give detailed advice. These leaflets are unanimous in advising that on no account should a double dose be given to make up for a missed dose. However, the vast majority of leaflets advise only on what to do if a single dose has been missed. Some leaflets advise taking the missed dose later (providing it is not too close to the next dose), whereas others recommend skipping the missed dose altogether and starting again with the next dose. In the event that more than one dose has been missed, the first question to ask is whether or not this is the appropriate drug for a patient to be taking. Poor compliance often indicates some dissatisfaction on the part of the patient. If it is a drug with a short half-life or one that requires lengthy re-titration, it may not be appropriate to restart prescribing for a patient who is frequently non-compliant. Similarly, if a patient is intoxicated with alcohol or drugs, it may not be sensible to restart medication at that time. Efforts should be made to find out if there are any particular reasons for non- compliance. Where poor adherence is a result of factors other than tolerability, consider the use of a long-acting injection (although these are only used, officially at least, in schizophrenia and schizoaffective disorder). When considering whether to restart the drug at the same dose as before or to re-titrate from a lower dose, the time since the last dose is vitally important. If more than a week or two has passed, then all drugs will probably need to be restarted as if it is new treatment (although for

many drugs that do not require titration this might mean starting back on the same dose as before). Exceptions include long-acting depot formulations and oral drugs with long half-lives such as aripiprazole, cariprazine and penfluridol. With these, there is a need to reload if the gap in treatment is very long, although shorter gaps (<2 weeks) might be managed by giving the usual dose and then reverting to the original dosing schedule. Lamotrigine must be considered separately from all other psychotropics because it has been associated with life-threatening cutaneous reactions, especially with high initial doses. The manufacturer's product information advises that if five half-lives have elapsed since the last lamotrigine dose was given, lamotrigine should be titrated as if for the first time. The half-life in healthy subjects on no other medication is around 33 hours. This is affected by other medications and is approximately 14 hours when given with glucuronidation-inducing drugs such as carbamazepine or phenytoin. The half-life is increased to approximately 70 hours when given with valproate. This means that the time before complete re-titration is necessary varies between 3 and 7 days, depending on other drugs co-prescribed.1 Table 14.4 summarises some very general recommendations. The drugs in the first column have specific safety issues that mean they require re-titration after the specified

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References

938 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 14 length of time. The drugs in the middle column are thought to be safe because the maximum dose is usually no higher than the highest recommended starting dose. The drugs in the right-hand column are thought to be safe to restart at the prior dose because a similar drug appears in the middle column, because clinical experience suggests they are safe or because the risks associated with giving untitrated high doses are thought to be low. Some suggestions are obtained from EU regulatory documents (SPCs),2 while others are mere suggestions based on clinical experience. If the gap in oral treatment is longer than 2 weeks, start as if it is new treatment (noting the exceptions listed earlier). References

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2. EMC. Summaries of Product Characteristics. 2024 (last accessed September 2024); https://www.medicines.org.uk/emc/. Table 14.4 Restarting medication up to 2 weeks after stopping oral treatment. Drugs that require re-titration Drugs that are usually safe for restarting at the previous dose Drugs that are possibly safe for restarting at the previous dose Drug Time after which re-titration must be performed Further guidance Clozapine 48 hours See section in Chapter 1 Acamprosate Asenapine Fluoxetine Haloperidol Isocarboxazid Lofepramine Methylphenidate Phenelzine Sulpiride Tranylcypromine Valproate Antipsychotics (exceptions in column 1) Carbamazepine (beware loss on enzyme induction) Cholinesterase inhibitors CNS stimulants Disulfiram Lithium (titration advised if renal function has changed) MAOIs Memantine Naltrexone Pregabalin SSRIs Lamotrigine 3–7 days See text Methadone, buprenorphine 3 days See section in Chapter 4 Paliperidone long-acting injection Depends on formulation See section in Chapter 1 Aripiprazole long-acting injection Depends on formulation See section in Chapter 1 Quetiapine Suggest 1 week Tolerance to sedative and hypotensive effects may be lost Risperidone Suggest 1 week Tolerance to hypotensive effects may be lost Tricyclics Suggest 1 week Tolerance to sedative and hypotensive effects may be lost MAOIs, monoamine oxidase inhibitors.

13 - Relational aspects of prescribing practice

Relational aspects of prescribing practice

14 - Object relations

Object relations

15 - Memory

Memory

16 - Treatment framework

Treatment framework

Prescribing psychotropics CHAPTER 14 Relational aspects of prescribing practice This section provides clinicians with practically useful advice in the relational aspects of prescribing. Evidence exists for the importance of the doctor–patient relationship in improving treatment outcomes.1–3 The key factors that help develop, maintain and deepen the relationship include instilling trust and regard.4 Three concepts are important here: object relations, memory and the treatment framework. Object relations This means how the individual views themselves and others around them. This view then influences how they process incoming data (e.g. what is happening in an interaction). This view of themselves has been determined from early experience. In essence it means that the present interaction may be experienced inaccurately through the prism of the past (another way to think of this experience is that this is the transference). This has implications for both the patient and the clinician. For example, if the patient has had early experience of uncaring parents, they will have greater difficulty in trusting the clinician. In turn, if the clinician's early experience is of demanding parents who expected them to always get it right, a treatment--resistant patient may be a particular challenge for them. This object relations approach allows one to be aware of factors regarding the patient, the clinician and the clinician– patient relationship. Memory Up to 95% of our goal-directed activities are executed unconsciously.5 Thus, the clinician's prescribing may be more influenced by procedural memory than their subjective view that they are using working memory (i.e. there is an illusion of the application of active thinking to solve the specificity of the present problem). By definition, procedural memory and the action flowing from this may not be best suited for a particular clinical situation. Acknowledging the unconscious influence on the present may help bring the conscious mind into play. Treatment framework This is using knowledge of the clinician's usual way of working (e.g. following this edition of The Maudsley Prescribing Guidelines), and a knowledge of how they tend to personally apply these guidelines. Straying from the guidelines may be based on good clinical judgement but also it may indicate that there is some psychological factor influencing decision-making. Given this psychological factor may be unconscious, the ability to review 'what one usually does' is then a useful check on what may be happening in prescribing. For example, if the prescriber is able to think 'I do not usually prescribe such a high dose of antipsychotic as a starting dose' they may then be able to pose the question 'Am I feeling very anxious to satisfy the demands of this patient?' In effect they may then be able to catch themselves acting out (i.e. replacing thinking with behaviour) in the countertransference (in this case their great anxiety to satisfy the patient).

17 - Factors that may influence the patients use o

Factors that may influence the patient’s use of and adherence to medication

940 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 14 Factors that may influence the patient’s use of and adherence to medication How the individual views themselves, and others, will influence many aspects of a person’s behaviour. These issues include their personal and cultural beliefs, readiness to change, ambivalence, expectations of treatment, attachment style and treatment preference. In addition, patients might use medication in countertherapeutic ways. We address each of these in turn in terms of their practical implications.6,7 Personal and cultural beliefs The religious, cultural and socioeconomic contexts shape our beliefs around concepts of illness, health and disability.8 Adherence to treatments is affected by the patient’s subjective beliefs and averages roughly 50% in almost all conditions.9 Recommendation: When it comes to prescribing within a culturally diverse population, prescribers need to reflect on their own cultural biases, enquire about the patient’s cultural beliefs, and work collaboratively with communities and families.10 Readiness to change Patients’ motivation and readiness to change can affect treatment outcomes. Beitman et al.11 examined stages of change and response to medication in patients with panic disorder and found that readiness to change was associated with better outcomes. The transtheoretical model12 proposes that people move through different stages of change and that interventions must match the stage of readiness. This model can also be useful for the treatment of other mental health conditions including personality disorder.13 Recommendation: The clinician’s appreciation of the stages of change, and the work involved in lasting change, can increase compassion and avoid wrongly timed interventions (including wrongly timed prescribing). A recovery-focused and patient-centred approach may help patients to understand entrenched patterns of behaviour, and to actively participate in behavioural change. Ambivalence Patients may worry about the safety of psychotropics, and mistrust clinicians. Further, symptoms may have an

adaptive and protective function thus making them harder for the patient to relinquish. For example, a patient who has elicited care might be ambivalent about getting better and losing this care. Recovery might portend, for example, confronting a difficult relationship or working through an intolerable loss.14 Recent advances in the field of neuropsychoanalysis suggest that unpleasurable feelings at a biological level indicate that the patient's underlying emotional needs are not being satisfied, serving as homeostatic 'error signals'. It is not a surprise then that symptoms (associated with feelings states) can be stubbornly resistant to symptom-focused treatments when the patient's basic emotional needs continue to be unmet.15 Recommendation: Exploring patients' ambivalence towards medication and healthcare professionals, and their previous experiences of care, can deepen the therapeutic relationship and is crucial in understanding patients' concerns. Understanding the

Prescribing psychotropics CHAPTER 14 patient's (often unconscious) underlying conflicts and motivations can explain symptom perseverance despite pharmacological endeavours. Acknowledgement of the patient's ambivalence during the recovery process may help validate their experience, facilitate rapport and enable conversations that the patient might otherwise be reluctant to approach. Expectations of treatment: placebo and nocebo effect Expectations of improvement or harm when taking medication exert a significant impact on treatment responses. The powerful 'placebo' response has been well described in medicine as a genuine psychobiological event.16 Conversely, expectations of harm are associated with negative treatment outcomes known as the 'nocebo' effect. Patients often expect harm from taking antidepressants, fearing dependence and loss of control of their emotions.17 Interestingly, patients who discussed adverse effects of antidepressants with their doctors were reported less likely to discontinue therapy than patients who did not discuss them.18 Recommendation: These findings emphasise the need to use all the elements of the therapeutic relationship in the care of patients.19 Clinical management of the nocebo effect includes awareness and recognition, focusing on the treatment alliance, carefully naming and working through mistrust, and careful disclosure of potential drug-related adverse effects, while remaining honest and clear.20 Attachment style Healthcare staff often represent attachment figures21 as they treat patients in times of need and distress. The attachment is particularly important when it comes to the management of long-term conditions. In one study, diabetic patients with dismissive attachment had significantly worse glucose control than patients with preoccupied or secure attachment style, but the effect was mitigated by improved communication between doctors and patients.22,23 Concerns about rejection, abandonment, control and intimacy24 are likely to affect patients' use of their medication. Patients with a dismissive attachment style may fear dependence on medication and services and not adhere to the prescribed interventions. Patients with a fearful-anxious attachment might need regular reassurance, while patients with a disorganised attachment might evoke disorganised and chaotic responses from healthcare staff. Recommendation: Consider attachment patterns when prescribing. Particular attention and consistency are needed to deliver coherent and reliable care alongside pharmacological interventions. Treatment preference The chronic illness model encourages consideration of the patient's treatment preferences. Research suggests that matching treatment to preference might improve outcomes for patients with depression.25 An RCT matching patients to treatment preference for major depressive disorder concluded that patients had better outcomes on their preferred treatment.26 These observations might apply to other conditions.

18 - Summary a checklist when prescribing

Summary – a checklist when prescribing

942 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 14 Recommendation: Consider treatment preference as one of the decision factors when prescribing. Countertherapeutic use of medication Medication (including overdose) may be used as a way of signalling submission, anger or helplessness. This is especially true in people who lack an emotional vocabulary and secure internal representations of benign care. Medication may become a way of self-management, replacing more developmental coping strategies and relationships. Recommendation: The clinician should consider the meaning of the emotional communication and be curious about alliance ruptures and system failures (and therefore reflect on the clinician's possible contributions to the rupture). Summary – a checklist when prescribing When faced with complex prescribing decisions, a checklist considering the discussed issues from the perspective of the patient, the clinician and the clinician–patient relationship may be helpful. The patient factor Q: 'What is my patient's story? What is my patient trying to communicate using words or, as important, through their actions in the here and now?' Recommendation: A formulation of the patient's underlying psychological difficulties may help. This may include: ■ ■Predominant relational pattern(s) – attachment style and relationship to care/ authority. ■ ■Ambivalence about symptoms – underlying psychological investment in status quo. ■ ■Meaning attached to medication and overall use of medication (including countertherapeutic use of medication). The clinician factor Q: 'How do I feel in response to my patient and how does that influence the action I am considering taking (e.g. do I feel helpless, frustrated, incompetent, guilty in the face of the patient's symptoms)? Am I prescribing to avoid unwanted feelings in my relationship with my patient?' Recommendation: 1 The first step in identifying countertransference pressure is to recognise and accept it, without always resorting to immediate action. 2 Self-review of practice. The clinician may ask: ■ ■Am I working within relevant guidelines? ■ ■Am I doing what I normally do (if not, am I being overly influenced by my countertransference)? ■ ■Do I have strong feelings about this patient? Do I have no feelings about this patient? (Which would be also worth considering.)

Prescribing psychotropics CHAPTER 14 ■ ■Are any circumstances different, for example do I have managers or other colleagues or the patient's family scrutinising me with this particular patient? 3

Seek support. Use supervision with colleagues and ask support from other members of the multidisciplinary team. It is important to work closely with colleagues (including pharmacists) to triangulate decisions when in complex prescribing dilemmas. Choosing to discuss a problem in supervision and outside of the heat of the consulting room can clarify thinking. The clinician–patient relationship Q: ‘What might prescribing a medication – or not prescribing – come to represent in my relationship with my patient?’ Limited consultation time and cancelled clinics might reinforce feelings of rejection and abandonment. Non-adherence to medication or overdose of prescribed medication might be a sign of a rupture in the clinician–patient relationship and further exploration can promote useful insights for patient and clinician. Recommendation: Consider the meaning of medication in the context of the patient, the clinician and the clinician–patient relationship. Cultivate a pharmacotherapeutic partnership and set limits:24 ■ ■Reframe prescribing as a partnership, rather than a one-directional activity of the doctor. ■ ■Provide, as much as possible, a stable and consistent consultation setting. ■ ■Set therapeutic limits, confronting unrealistic expectations of care. (This includes maintaining a realistic humility around the limitations of psychopharmacology, and psychoeducating patients regarding what medications can and cannot achieve and their place in the overall journey to recovery and development.) ■ ■Endorse a stance that can promote the pharmacotherapeutic alliance, characterised by emotional presence and warmth, good and honest communication, and support of the patient’s autonomy and agency. This includes shared decision-making and respect for the patient’s treatment preferences, when clinically indicated. ■ ■Openly discuss overall recovery goals, target symptoms, duration of treatment and potential adverse effects, and address any associated anxieties. ■ ■A clear agreement on treatment objectives, consistent with the overall care plan, and the respective responsibilities of doctor and patient can promote agency and strengthen the pharmacotherapeutic partnership. ■ ■Collaborative crisis planning should be part of this, especially when there are risk concerns.

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20 - Prescribing drugs outside their licensed indi

Prescribing drugs outside their licensed indications (‘off-label’ prescribing)

Prescribing psychotropics CHAPTER 14 Prescribing drugs outside their licensed indications (‘off--label’ prescribing) A Product Licence is granted when regulatory authorities are satisfied that the drug in question has proven efficacy in the treatment of a specified disorder, along with an acceptable adverse effect profile, relative to the severity of the disorder being treated and other available treatments. Licensed indications are preparation- specific, outlined in the SPCs, and may be different for branded and generic formulations of the same drug.1 In the USA, product ‘labelling’ has a similar legal status to EU licensing. The decision of a manufacturer to seek a Product Licence for a given indication is essentially a commercial one. Potential sales are balanced against the cost of conducting the necessary clinical trials. Drugs may be effective outside their licensed indications for different disease states, age ranges, doses and durations. The absence of a formal Product Licence or labelling may reflect the absence of controlled trials supporting the drug’s efficacy in these areas. In some cases (e.g. sertraline or quetiapine in generalised anxiety disorder [GAD]) there is sufficient evidence but a licence has not been sought by the manufacturer. Importantly, however, it is also possible that trials have been conducted but have given negative or equivocal results. Clinicians often assume that drugs with a similar mode of action will be similarly effective for a given indication. This may encourage the assumption that the official labelling for one drug indicates efficacy and safety of another, similar drug. However, apparently similar drugs may differ in respect to active metabolites and in regard to receptor affinity. Prescribing a drug within its licence or labelling does not guarantee that the patient will come to no harm. Likewise, prescribing outside a licence does not mean that the risk–benefit ratio is automatically adverse. For example, sertraline and fluoxetine are no less effective for GAD than alternative, licensed drugs.2 Prescribing outside a licence, usually called ‘off-label’, does confer extra responsibilities on prescribers, who will be expected to be able to show that they acted in accordance with a respected body of medical opinion (the Bolam test)3 and that their action was capable of withstanding logical analysis (the Bolitho test).4 In the UK, both have effectively been superseded, or at least clarified, by the

Montgomery vs Lanarkshire Health Board appeal case decision5 which stated: An adult person of sound mind is entitled to decide which, if any, of the available forms of treatment to undergo, and her consent must be obtained before treatment interfering with her bodily integrity is undertaken. The doctor is therefore under a duty to take reasonable care to ensure that the patient is aware of any material risks involved in any recommended treatment, and of any reasonable alternative or variant treatments. The test of materiality is whether, in the circumstances of the particular case, a reasonable person in the patient's position would be likely to attach significance to the risk, or the doctor is or should reasonably be aware that the particular patient would be likely to attach significance to it. Thus, in the UK at least, the prescriber has a duty to make a patient aware of any material risks associated with the prescribing of any medicines and to outline alternatives.

946 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 14 The General Medical Council allows doctors to prescribe off-label but only where the prescriber is satisfied that there is enough evidence or experience to support efficacy and safety.6 In the USA, it is lawful to prescribe off-label 'within a legitimate health care practitioner–patient relationship'.7 Marketing of off-label use is forbidden but information may be provided following an unsolicited request.8 Off-label prescribing represents a significant proportion of prescribing in mental health conditions in the USA.9,10 A similar degree of off-label prescriptions is seen in other countries.11–13 Off-label prescribing in psychiatry is less likely to be supported by a strong evidence base than off-label prescribing in other areas of medicine.14 In psychiatry, small (underpowered) studies (with wide confidence intervals) often influence practice, particularly with respect to treatment-resistant illness (a great many examples can be found in this book). When these small studies are combined in the form of a meta-analysis, considerable heterogeneity is often found, suggesting publication bias (i.e. that some negative studies are not published). Treatments may therefore become incorporated into 'routine custom and practice' in the absence of robust evidence supporting efficacy and/or tolerability, and these treatments may sometimes continue to be used despite the findings of later, larger and more definitive negative studies and meta-analyses. An example of widespread off-label prescribing of a psychotropic in non-mental health conditions is amitriptyline – 93% of UK primary care prescriptions are off-label.15 The psychopharmacology special interest group at the Royal College of Psychiatrists published a consensus statement on the use of licensed medicines for unlicensed uses.16 They noted that unlicensed use is common in general adult psychiatry, with cross- sectional studies showing that up to 50% of patients are prescribed at least one drug outside the terms of its licence. They also note that the prevalence of this type of prescribing is likely to be higher in patients under the age of 18 or over 65, in those with a learning disability, in women who are pregnant or lactating and in those patients who are cared for in forensic psychiatry settings. The main recommendations in the consensus statement are summarised in Box 14.1. Box 14.1 Recommendations before prescribing 'off-label' ■ ■Exclude licensed alternatives (e.g. they have proved ineffective or poorly tolerated). ■ ■Ensure familiarity with the evidence base for the intended unlicensed use. If unsure, seek advice from another clinician (and possibly a specialist pharmacist). ■ ■Consider and document the potential risks and benefits of the proposed treatment. Share this risk assessment with the patient, and carers if applicable. Document the discussion and the patient's consent or lack of capacity to consent. ■ ■If prescribing responsibility is to be shared with primary care, ensure that the risk assessment and consent issues are shared with the GP. ■ ■Monitor for efficacy and adverse effects; start a low dose and increase slowly. ■ ■Consider publishing the case to add to the body of knowledge. ■ ■Withdraw any treatment that is ineffective or where emergent risks outweigh the benefits. The more experimental the

unlicensed use is, the more important it is to adhere to the above guidance.

21 - Examples of acceptable use of drugs outside t

Examples of acceptable use of drugs outside their licences/labels

Prescribing psychotropics CHAPTER 14 The advice is largely echoed by more recent publications from the American Psychiatric Association17 (who note that off-label prescribing should be reimbursed) and the Royal Australian and New Zealand College of Psychiatrists18 who emphasise shared decision-making and the presumption of capacity. Examples of acceptable use of drugs outside their licences/labels Table 14.5 gives examples of common unlicensed uses of drugs in psychiatric practice. These examples would all fulfil the Bolam and Bolitho criteria in principle. An exhaustive list of unlicensed uses is impossible to prepare as the evidence base is constantly changing and because the expertise and experience of prescribers vary. A particular strategy may be justified in the hands of a specialist in psychopharmacology based in a tertiary referral centre but be much more difficult to justify if initiated by someone with a special interest in psychotherapy who rarely prescribes. Note that some drugs do not have a UK licence for any indication. Two commonly prescribed examples in psychiatric practice are immediate-release formulations of melatonin (used to treat insomnia in children and adolescents) and pirenzepine (used to treat clozapine-induced hypersalivation). Awareness of the evidence base and documentation of potential benefits, adverse effects and patient consent are especially important here. Table 14.5 Examples of common unlicensed uses of drugs in psychiatric practice. Drug/drug group Unlicensed use(s) Further information Second-generation antipsychotics Psychotic illness other than schizophrenia Licensed indications vary markedly, and in most cases are unlikely to reflect real differences in efficacy between drugs. Clozapine Bipolar disorder Substantial evidence to support efficacy when standard treatments have failed to control symptoms Cyproheptadine Akathisia Some evidence to support efficacy in this distressing and difficult to treat adverse effect of antipsychotics Fluoxetine/sertraline Generalised anxiety disorder Substantial supporting evidence Ketamine (racemate) Refractory depression Substantial evidence with both racemate and S-isomer Melatonin (circadin) Insomnia in children Licence covers adults >55 years only. Probably preferable to unlicensed formulations of melatonin. Naltrexone Self-injurious behaviour in people with learning

disabilities Limited evidence base Acceptable in specialist hands Sodium valproate Treatment and prophylaxis of bipolar disorder Established clinical practice Evidence from other valproate preparations

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23 - The Mental Health Act in England and Wales

The Mental Health Act in England and Wales

Prescribing psychotropics CHAPTER 14 The Mental Health Act in England and Wales The 1983 Mental Health Act (MHA) as amended by the 2007 MHA is the legislation within England and Wales that provides the framework for detaining and treating people with mental disorder in hospital. It also allows for the supervision of people in the community. Mental health law as it pertains to other countries is not covered in this book. The guidance here provides a quick summary of the sections that prescribers are likely to come across in their day-to-day work (Box 14.2). It is not an exhaustive list. The Act has a statutory Code of Practice for practitioners and Chapter 25 of the Code provides detailed guidance on the treatment rules of the Act.1 The MHA can be accessed at www.legislation.gov.uk. The power to treat under S58 is only for treatment of mental disorder. Physical treatment (generally) is governed by the normal rules of consent or, if the person lacks capacity, the authority of the Mental Capacity Act. The Responsible Clinician (RC) is usually the patient's consultant. For the first 3 months of detention, the RC may give medication with or without consent to a person under one of the detention sections named for the treatment of their mental disorder. Thereafter, the patient's consent or a second opinion must be sought. The 3 months' countdown starts when medication for mental disorder is first administered while the patient is detained. This includes a patient detained under S2 who is then, without a break, detained under S3. For practical purposes the 3-month rule is usually calculated from the date of first detention. Box 14.2 Civil and forensic detention sections Section 2 Admission for assessment which lasts for up to 28 days Section 3 Admission for treatment which may last up to 6 months and is renewable Section 36 Remand to hospital for treatment Section 37 Hospital Order made by the courts (runs like an S3) Notional 37 Treat as if subject to S37. This term is used informally under a number of different circumstances. One example is where a patient was previously detained under S47/49 and their restriction order expires. Section 38 Interim Hospital Order Section 41 Restriction order: an order made by the Crown Court restricting discharge. Accompanies S37 and is written as S37/41. Section 47 Transfer to hospital of prisoners Section 49 A restriction order which usually accompanies S47 (written as S47/49) Section 48 Applies to unsentenced prisoners in need of urgent treatment and is accompanied by S49 (written as S48/49) Section 58 Treatment requiring consent or a second opinion Please note in law it is the Responsible Clinician (RC) who is accountable for the operation of S58

24 - Completion of forms T2 and T3

Completion ofÂ forms T2 andÂ T3

25 - Arranging and preparing for SOAD visits

Arranging and preparing for SOAD visits

26 - Statutory consultees

Statutory consultees

950 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 14 If a patient consents to treatment, the RC completes a form T2. If a patient has not given consent or has not got the capacity to consent, a Second Opinion Appointed Doctor (SOAD) is called. The SOAD then completes a form T3. A copy of the forms T2 and T3 should be kept with the patient's medication chart as recommended in paragraph 25.75 of the Code of Practice.1 Completion of forms T2 and T3 The following should be stated on the forms: ■ ■The name of the drug or the class of drug. ■ ■If the class of drug is stated, the number of drugs allowed at any one time. ■ ■The route of administration. ■ ■The maximum dosage with reference to BNF guidance. For example: Antipsychotic,second generation 1 oral within B ( ) × NF maximum dose limits. For a patient who has capacity and is consenting to treatment and is only willing to take a particular drug, it is appropriate for the RC to write the name of the drug instead of the name of the class of drug on the T2. For example: Olanzapine tablets only(oral)within BNF maximum dose limits. Psychotropics not found in the BNF may be written on a T2 or T3 with their indication. For example: Melperone tablets oral up to a maximum of 25mg dai ( )

ly for the treatment of schizophrenia.

Non-psychotropics used for the treatment of mental disorder should be included on the T2 and T3, for example omega-3 fatty acids (fish oils) in schizophrenia. Antimuscarinics used to treat hypersalivation and the extrapyramidal side effects of antipsychotics should be included too. Arranging and preparing for SOAD visits The Code of Practice 25.51 states: 'Clinicians should consider seeking a review by a specialist mental health pharmacist before seeking a SOAD certificate, particularly if the patient's medication regime is complex or unusual.' Statutory consultees The SOAD should consult with two people before issuing a T3. One must be a nurse. The other must not be a nurse or a doctor. Both must have been involved with the patient's treatment. These two people are known as statutory consultees. Mental health pharmacists can perform this role where they have been involved in any recent review of a patient's medication.

27 - What is consent

What is consent?

28 - What is capacity

What is capacity?

Prescribing psychotropics CHAPTER 14 The Code of Practice 25.56 states: Statutory consultees may expect to have a private discussion with the SOAD and to be listened to with consideration. Issues that the consultees may be asked about include, but are not limited to: ■ ■the proposed treatment and the patient's ability to consent to it; ■ ■their understanding of the past and present views and wishes of the patient; ■ ■other treatment options and the way in which the decision on the treatment proposal was arrived at; ■ ■the patient's progress and the views of the patient's carers; and ■ ■where relevant, the implications of imposing treatment on a patient who does not want it and the reasons why the patient is refusing treatment. What is consent? The Code of Practice 24.34 defines consent as: … the voluntary and continuing permission of a patient to be given a particular treatment, based on a sufficient knowledge of the purpose, nature, likely effects and risks of that treatment, including the likelihood of its success and any alternatives to it. Permission given under any unfair or undue pressure is not consent. For a patient to consent formally they must have the 'capacity' to make a decision. What is capacity? The Mental Capacity Act 2005 states that: ■ ■People must be assumed to have capacity unless it is established that they lack capacity. ■ ■People are not to be treated as unable to make a decision unless all practicable steps to help them do so have been taken without success. ■ ■People are not to be treated as unable to make a decision merely because they make an unwise decision. A patient is deemed to lack capacity if they cannot: ■ ■Understand relevant information about the decision to be made; or ■ ■Retain that information in their mind; or ■ ■Use or weigh that information as part of the decision-making process; or ■ ■Communicate their decision (by talking, using sign language or any other means). The patient needs to fail on only one of the four points above to be deemed not to have capacity. Capacity may change over time so reassessment is important. A person may lack capacity about one decision but not about another.

29 - Section 62 urgent treatment

SectionÂ 62 urgent treatment

30 - Section 132 duty of managers of hospitals to

Section 132 duty of managers of hospitals to give information to detained patients

31 - Electroconvulsive therapy (ECT)

Electroconvulsive therapy (ECT)

952 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 14 Section 62 urgent treatment If after 3 months medication is needed urgently to treat a patient’s mental disorder and it is not covered by a T2 or T3, S62 may be applied. The Code of Practice 25.38 states: This applies only if the treatment in question is immediately necessary to: ■ ■save the patient’s life; ■ ■prevent a serious deterioration of the patient’s condition, and the treatment does not have unfavourable physical or psychological consequences which cannot be reversed; ■ ■alleviate serious suffering by the patient, and the treatment does not have unfavourable physical or psychological consequences which cannot be reversed and does not entail significant physical hazard; or ■ ■prevent patients behaving violently or being a danger to themselves or others, and the treatment represents the minimum interference necessary for that purpose, does not have unfavourable physical or psychological consequences which cannot be reversed and does not entail significant physical hazard. Each Trust should design a form for the clinician in charge of treatment (usually the consultant) to state what the treatment is, why it is immediately necessary and the length of treatment. Section 132 duty of managers of hospitals to give information to detained patients With regard to S132 and consent to treatment the Code of Practice 4.20 states: Patients must be told what the Act says about treatment for their mental disorder. In particular they must be told: ■ ■the circumstances (if any) in which they can be treated without their consent – and the circumstances in which they have the right to refuse treatment; ■ ■the role of second opinion appointed doctors (SOADs) and the circumstances in which they may be involved; and ■ ■(where relevant) the rules on electroconvulsive therapy (ECT) and medication administered as part of ECT. Electroconvulsive therapy (ECT) Section 58a deals with ECT. Treatment for ECT is authorised on forms: T4 For consenting adults 18 and over, may be written by the RC or SOAD T5 For consenting patients under 18, to be written by SOAD only T6 For patients who lack capacity, to be written by SOAD only

32 - Community patients

Community patients

33 - Reference

Reference

Prescribing psychotropics CHAPTER 14 All patients under the age of 18 who are to receive ECT, whether or not they are detained under the MHA, must have treatment authorised on a T5 or T6. Patients who have the capacity to consent must not receive ECT unless they do consent (in emergencies this can, however, be over-ridden under S62 of the Act). There is no 3-month rule with regard to ECT and this also applies to medication given as part of ECT. Hence a form for ECT must always be in place regardless of the first date of detention. The forms should indicate the maximum number of treatments the patient is to receive (Code of Practice paragraph 25.23). Community patients Patients on a Community Treatment Order (CTO) should have treatment authorised on one of the following forms: CTO11 Written by SOAD, after 1 month on a CTO, when the patient lacks capacity CTO12 Written by the RC when the patient has capacity and is consenting to treatment, after 1 month on a CTO There is no legal authority to give patients medication in the community if they refuse it. Reference

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34 - Site of administration of intramuscular injec

Site of administration of intramuscular injections

954 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 14 Site of administration of intramuscular injections Table 14.6 gives the sites of administration formally permitted in the individual product’s EU licence. Other routes and sites may be possible but pharmacokinetic analysis of administration via these sites is generally not available. Table 14.6 Sites of administration of intramuscular injections. Antipsychotic generic name and formulation Licensed site(s) of administration Typical antipsychotic (FGA) depots Bromperidol decanoate in sesame oil (available in Belgium, Germany, Italy, Luxembourg and the Netherlands1,2) Deep intramuscular injection into the gluteal muscle. SPCs in some countries recommend to alternate injections into the left and right sides to prevent pain at the injection site.3 Flupentixol decanoate in thin vegetable oil derived from coconuts Deep intramuscular injection into the upper outer buttock (dorsogluteal) or lateral thigh (vastus lateralis).4 As with all oil-based injections it is important to ensure, by aspiration before injection, that inadvertent intravascular entry does not occur.5 This probably applies to dorsogluteal injections only; for all other sites where there are no major blood vessels close to the injection site, this is unnecessary.4 Fluphenazine decanoate in sesame oil Deep intramuscular injection into the gluteal region.4 Has also been administered into the lateral surface of the thigh muscle but this is unlicensed. Administration into the deltoid is not recommended by manufacturer.6 In the USA, licensed to be used ‘intramuscularly or subcutaneously’. The site of administration is not specified. Drug leakage appears to be lower after SC injection than after intramuscular administration.7 Fluspirilene in vegetable oil8 (available in some EU countries, Canada, Argentina and Israel9) Deep intramuscular injection into the gluteal muscle (intragluteal). Because of its microcrystalline form, irritation and inflammation symptoms may occur at the injection site. Manufacturer recommends to alternate between left and right gluteal muscles.3,10 Haloperidol decanoate in sesame oil Deep intramuscular injection into the gluteal region.4 It is recommended to alternate between the two gluteal muscles.11 As the administration of volumes greater than 3mL is uncomfortable for the patient, such large volumes are not recommended.11,12 Can also be administered into the deltoid muscle according to the manufacturer.13 Although this is an unlicensed use, one trial suggests it is safe and effective.14 Perphenazine decanoate in sesame oil (used in the Nordic countries, Belgium, Portugal and the Netherlands15) Deep intramuscular injection.15,16 No other information available.

Table 14.6 (Continued) Antipsychotic generic name and formulation Licensed site(s) of administration Perphenazine enanthate in sesame oil (in clinical use in the Nordic countries, Belgium, Portugal and the Netherlands15) Pipotiazine palmitate in sesame oil4 (variable availability) Zuclopenthixol decanoate in thin vegetable oil derived from coconuts Atypical antipsychotic (SGA) depots Gluteal muscle administration4 Aripiprazole Prefilled syringe for prolonged-release suspension Aripiprazole lauroxil Prefilled syringe for extended-release suspension Aripiprazole lauroxil nanocrystal dispersion Prefilled syringe for extended-release suspension Olanzapine pamoate monohydrate Powder and vehicle for prolonged-release suspension Paliperidone palmitate 1-monthly Prolonged-release suspension for injection every month Prescribing psychotropics Deep intramuscular injection into the gluteal region.15,17 Administration should be by deep intramuscular injection into the gluteal region.18 Deep intramuscular injection into the upper outer buttock (dorsogluteal) or lateral thigh (vastus lateralis).4 As with all oil-based injections it is important to ensure, by aspiration before injection, that inadvertent intravascular entry does not occur.19 Gluteal injections should be alternated between the two gluteal muscles. Deltoid muscle administration4,20 Deltoid injections should be alternated between the two deltoid muscles.20 The powder and vehicle vials and the prefilled syringe are for single use only.4 Intramuscular administration into the deltoid or gluteal (441mg dose only) muscle.4,21 CHAPTER 14 Intramuscular injection into the deltoid or gluteal muscle.22 Not intended for repeat dosing. Given as a single dose to initiate treatment with aripiprazole lauroxil.22 Olanzapine pamoate monohydrate should only be administered by deep intramuscular gluteal injection by a healthcare professional trained in the appropriate injection technique and in locations where post-injection observation and access to appropriate medical care in the case of overdose can be assured.23 Injected slowly, deep into the deltoid or dorsogluteal muscle (the two initial loading doses should be administered in the deltoid muscle so as to attain therapeutic concentrations rapidly).4,24 Following the second initiation dose, monthly maintenance doses can be administered in either the deltoid or gluteal muscle. Administration should be in a single injection. The dose should not be given in divided injections.24 (Continued)

 Table 14.6 (Continued) Antipsychotic generic name and formulation Licensed site(s) of administration Paliperidone palmitate 3-monthly Prolonged-release suspension for injection every 3 months Deltoid muscle administration25 The specified needle for administration of Trevicta into the deltoid muscle is determined by the patient’s weight (see manufacturer’s advice). It should be administered into the centre of the deltoid muscle. Deltoid injections should be alternated between the two deltoid muscles. Gluteal muscle administration25 To be administered into the upper outer quadrant of the gluteal muscle. Gluteal injections should be alternated between the two gluteal muscles. Paliperidone palmitate 6-monthly Prolonged-release suspension for injection every 6 months Byannli is for gluteal intramuscular use only. It must not be administered by any other route. Each injection must be administered only by a healthcare professional giving the full dose in a single injection. It should be injected slowly, deep into the upper outer quadrant of the gluteal muscle. A switch between the two gluteal muscles should be considered for future injections in the event of injection site discomfort. Needles from the 3-monthly or 1-monthly paliperidone palmitate injectable pack or other commercially available needles must not be used when administering Byannli.26 Risperidone microspheres (Consta) Powder and vehicle for prolonged-release suspension Following reconstitution, administer via deep intramuscular deltoid or gluteal injection.27 Risperidone ISM (Okedi) Powder and solvent for extended-release suspension After

reconstitution, administer by deep intramuscular deltoid or gluteal injection.28 Risperidone 2-weekly injection (Rykindo) Prefilled syringe and powder vial for prolonged-release suspension After reconstitution, administer via intramuscular injection into the gluteal muscle.29 Risperidone subcutaneous long-acting injections (Perseris [RBP-7000], Uzedy [TV-46000]) Extended-release suspension Subcutaneous administration in the abdomen or upper arm.30,31 Prior to administration of Perseris (RBP-7000), the liquid and powder syringes need to be mixed by passing the contents back and forth between the syringes. Intramuscular injections for rapid tranquilisation Aripiprazole Solution for injection To enhance absorption and minimise variability, injection into the deltoid or deep within the gluteus maximus muscle, avoiding adipose regions, is recommended.32 Haloperidol Solution for injection Intramuscular administration.33 Preferably, the gluteal muscle is selected when the dosage volume is high. The deltoid muscle is preferred for low doses of the injection. However, there is no information on the dosage limit for these specific muscle groups. Choice of site is at the discretion of the prescriber according to the manufacturer.34

35 - References

References

Prescribing psychotropics CHAPTER 14 Table 14.6 (Continued) Antipsychotic generic name and formulation Licensed site(s) of administration Lorazepam Solution for injection Intramuscular administration. Can be administered into the gluteal, deltoid or frontal thigh area according to the manufacturer.35 A 1:1 dilution of Ativan injection with normal saline or Sterile Water for Injection BP is recommended in order to facilitate intramuscular administration and absorption.18 Olanzapine Powder for solution for injection Inject slowly, deep into the muscle mass. The exact site of administration is not specified and choice of muscle site should be a clinical decision according to the manufacturer.36 Not to be used intravenously* or subcutaneously. Use the solution immediately within 1 hour of reconstitution.37 *Intravenous use has been reported38,39 but is off-licence/label. Promethazine hydrochloride Solution for injection By deep intramuscular injection into a large muscle.40 Can be administered into the thigh, upper arm or gluteal region. Ensure muscle mass is sufficient for the volume being injected.6 Other intramuscular injections Clotiapine 40mg/4mL injection (available in Argentina, Belgium, Israel, Italy, Luxembourg, South Africa, Spain, Switzerland and Taiwan41) By intramuscular injection.41 No other information available. Clozapine intramuscular injection 25mg/mL (unlicensed)42,43 Only for deep intramuscular administration into the gluteal muscle. 25mg IM clozapine = 50mg oral. The maximum volume that can be injected into each site is 4mL (100mg). For doses greater than 100mg daily, the dose may be divided and administered into two sites. (Injection sites should be rotated as per usual IM practice.) Administration into the lateral thigh and deltoid muscles has been used in one case series.42 FGA, first-generation antipsychotic; ISM, in situ microparticles; SC, subcutaneous; SGA, second-generation antipsychotic; SPC, summary of product characteristics. References

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