03 - Summary of psychiatric adverse effects of non

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Miscellany CHAPTER 15 Summary of psychiatric adverse effects of non-psychotropics It is increasingly recognised that non-psychotropic medications can induce a wide range of psychiatric symptoms.1 Up to two-thirds of all drugs have potential psychiatric adverse effects listed in their product labelling,2 although in most cases the evidence supporting a causal link is limited. Psychiatric adverse effects are poorly characterised in drug clinical trials, often only becoming apparent during post-marketing surveillance.3 Given this level of uncertainty, suspected psychiatric adverse effects should be diagnosed and managed on a case-by-case basis. As a general guide, the psychiatric adverse effects of non-psychotropics are shown in Table 15.3. For individual drugs and agents not listed in this table, additional sources of information and the product literature should be consulted. Note that psychiatric adverse effects of drugs used in psychiatry and drugs for human immunodeficiency virus (HIV) and epilepsy are summarised elsewhere in this book. Table 15.3 Summary of psychiatric adverse drug reactions (ADRs) with non-psychotropics.4–7 Drug Psychiatric adverse effect Comment Analgesics Opioids Sedation, dysphoria, confusion, mood changes including euphoria, sleep disturbances, hallucinations, psychosis, delirium, dependence Psychiatric ADRs are relatively common with opioids. Psychosis during opioid withdrawal has also been reported rarely.8 5HT1 agonists (e.g. sumatriptan) Fatigue, anxiety, panic attacks Antibiotics Cephalosporins, penicillins, quinolones (including fluoroquinolones), tetracyclines Sleep disturbances (insomnia and somnolence, abnormal dreams, nightmares), anxiety, delirium and confusional states, depression and agitation, psychotic symptoms (e.g. hallucinations, suicidal ideation) All antibiotics can cause delirium. Patients with underlying medical conditions can be at higher risk of developing psychiatric ADRs. Of the quinolones, ciprofloxacin causes the most psychiatric ADRs, including mood disturbances, agitation and confusion. Onset of psychiatric ADRs can be fast, e.g. after one dose. Isoniazid9 Mania, psychosis Mood-elevating properties have long been noted. In rare cases has been associated with

the emergence of manic/psychotic symptoms. Antimalarials Chloroquine, mefloquine Psychosis including hallucinations, panic attacks, suicidal ideation and attempts, anxiety, depression, restlessness, confusion. Abnormal dreams/nightmares are common with mefloquine. Symptoms begin early in treatment. Patients should be advised to stop treatment if these develop and seek medical advice. Psychiatric ADRs are more common with mefloquine than chloroquine. Reactions can even occur after discontinuation of the drug. Mefloquine should not be prescribed for patients with an active or a history of a psychiatric diagnosis. (Continued)

970 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 15 Table 15.3 (Continued) Drug Psychiatric adverse effect Comment Antiparkinsonian treatments Levodopa Visual hallucinations, depression, hypomania, sleep disturbances, abnormal dreams, cognitive impairment, agitation, psychosis, delirium Dopamine agonists Sedation, psychomotor agitation, anxiety, akathisia, sleep disturbances, psychosis, cognitive impairment, delirium, visual hallucinations These are associated with more psychiatric adverse effects than levodopa Amantadine Decreased concentration, sleep disturbances, visual hallucinations, irritability, anxiety, depression, euphoria, fatigue, psychosis, delirium Selegiline (MAO-B inhibitor) Sleep disturbances, agitation, psychosis Primary metabolites include levamfetamines Entacapone (COMT inhibitor) Sleep disturbances, hallucinations, delirium Cardiovascular agents ACE inhibitors (e.g. captopril, lisinopril) Fatigue, hallucinations, delirium, mood disturbances Captopril most strongly associated with mood effects. Overall limited psychiatric ADRs. Beta-blockers Fatigue, sedation, sleep disturbances and nightmares, cognitive impairment, depression, hallucinations, psychosis, delirium Disturbances more common with lipophilic beta-blockers (e.g. propranolol, metoprolol) than with hydrophilic beta-blockers (e.g. atenolol, sotalol, nadolol). Propranolol most commonly associated with depressive symptoms, but even with this drug causality has not clearly been established. Reports of psychiatric ADRs from numerous clinical trials are equivocal. Calcium channel blockers (e.g. diltiazem, amlodipine) Mood changes, lethargy, dysphoria, mania, psychosis, delirium, akathisia Causal association not clearly demonstrated Statins10–12 (e.g. simvastatin, atorvastatin) Cognitive impairment, memory impairment, depression, emotional lability, irritability, sleep disturbance Causal associations between statins and changes in mood, sleep and cognition have not been established in systematic reviews of RCTs. Statins penetrate the blood–brain barrier; simvastatin has the highest permeability. Switching to hydrophilic statins (e.g. pravastatin, rosuvastatin) has been suggested in suspected cases of moderate to severe psychiatric ADRs.

Miscellany CHAPTER 15 Table 15.3 (Continued) Drug Psychiatric adverse effect Comment Corticosteroids Glucocorticoids (e.g. betamethasone, prednisolone, prednisone) Mood disorders, mania/ hypomania (particularly with higher doses),13 suicidal ideation, euphoria, agitation, sleep disturbances, psychosis and delirium, dementia, cognitive impairment Clear causal association. Most substantial associations are with depression and mania.14 Onset of psychiatric ADRs is often very sudden, and within the first 1–2 weeks of starting treatment. Symptoms generally respond to dose decreases and have been reported in association with several routes of administration (including oral, parenteral and inhaled), although are probably less common with inhalation. Symptoms usually resolve on gradual discontinuation, although duration of symptoms varies considerably. Other agents 5α-reductase inhibitors (e.g. finasteride)15 Depression, anxiety, suicidality A pharmacovigilance database study of finasteride found associations with suicidality and other psychological adverse events in younger patients receiving treatment for alopecia but not older patients receiving treatment for BPH.16 Chemotherapeutic agents (e.g. 5-fluorouracil, asparaginase, bortezomib, ifosfamide, vincristine) More commonly: cognitive impairment, delirium,

psychosis Less commonly: depression, anxiety, suicidal ideation Almost all chemotherapeutic agents are associated with significant psychiatric ADRs, which may be multifactorial in origin (i.e. secondary to the disease process, ADRs and psychological distress). Cancer therapy- associated cognitive changes include difficulty in executive functions, multitasking, short-term memory recall and attention. Cognitive changes seem to be dose- dependent, and certain drugs (methotrexate, fludarabine, cytarabine, 5-fluorouracil, cisplatin) are associated with worse cognitive effects. Cimetidine Cognitive impairment, delirium Interferons-α and -β Depression, loss of efficacy of previously effective antidepressants, suicidal ideation, delirium, non-specific psychiatric symptoms. Rare case reports of psychosis and mania with interferon-α. Psychiatric ADRs are relatively unlikely with interferon-β but much more widely reported with interferon-α. Interferon-α-associated depression responds to antidepressants, use of which can be preventative. Novel diagnostic biomarkers have been investigated to predict which patients are likely to develop interferon-α--associated psychiatric ADRs. (Continued)

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