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Summary

Schizophrenia and related psychoses CHAPTER 1 Clozapine and chemotherapy The use of clozapine with agents that cause neutropenia is formally contraindicated. Most chemotherapy treatments cause significant bone marrow suppression. When the white blood cell count drops below 3.0×109/L clozapine is usually discontinued. This is an important safety precaution outlined in the formal licence/labelling. For many regimens it can be predicted that chemotherapy will reduce the white blood cell (WBC) count below this level, irrespective of the use of clozapine. The use of chemotherapy may be more likely in people taking clozapine because of its association with malignancy.1,2 Ideally, clozapine should be discontinued before chemotherapy starts. However, this will place most patients at high risk of relapse or at least significant deterioration of their psychotic illness, which may then affect their capacity to consent to chemotherapy. This poses a therapeutic dilemma in patients prescribed clozapine and requiring chemotherapy. In practice, most patients do continue on clozapine treatment during chemotherapy. Liaison with regulatory bodies is essential in ensuring continuity of clozapine treatment for patients who are also receiving chemotherapy. Severe clozapine-induced neutropenia is very rare in people taking clozapine for longer than a year, while neutropenia is a known adverse effect of many chemotherapy regimens. Chemotherapy has a predictable effect on neutrophil counts, both in terms of magnitude of effect and the timing, so knowledge of these factors should help determine the cause of any neutropenia that develops. There are a number of case reports supporting continuing clozapine during chemotherapy,3–18 but interpretation of this literature should take account of possible publication bias.3 Before initiating chemotherapy for a patient receiving clozapine, it is essential to put in place a treatment plan that is agreed with all relevant healthcare staff involved and, of course, the patient and family members/carers. This will include the oncologist/ physician, psychiatrist, haematologist, pharmacist and the clozapine monitoring service. Plans should be made in advance for the action that should be taken when the WBC count drops below the normally accepted minimum. This plan should cover the frequency of haematological monitoring, increased vigilance regarding the clinical consequences of neutropenia/agranulocytosis, if and when clozapine should be stopped, and the place of medication such as lithium and G-CSF19,20 to try and support the maintenance of normal neutrophil counts. In the UK, the clozapine monitoring service will normally ask the psychiatrist to sign an ‘unlicensed use’ form and will request additional blood monitoring. Complications appear to be rare but there is one case report of neutropenia persisting for 6 months after doxorubicin, radiotherapy and clozapine.6 G-CSF has been used to treat agranulocytosis associated with chemotherapy and clozapine in combination.7,8,21 As discussed above, the risks of life-threatening blood dyscrasia are probably lowest in those who have received clozapine for longer than a year, in whom a clozapine-induced severe neutropenia would be highly unusual. Summary ■ ■If possible, clozapine should be discontinued before starting chemotherapy but, for

almost all people, the risk–benefit analysis will be judged to be in favour of continuing clozapine.

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