Dear Colleague

CLOZAPINE AND GASTROINTESTINAL OBSTRUCTION

Clozapine is indicated for the treatment of schizophrenia (including psychosis in Parkinson’s disease) in patients unresponsive to, or intolerant of, conventional antipsychotic drugs. Recognised fatal adverse effects include agranulocytosis, myocarditis and cardiomyopathy. Clozapine-induced gastrointestinal hypomotility is probably less well recognised but can progress to severe and fatal bowel obstruction. The recent death of an individual from clozapine-induced constipation, exacerbated by co-administration of the anticholinergic agent pirenzepine, has triggered a request from the coroner (under Rule 43) to take appropriate action and avoid similar adverse events recurring. The purpose of this letter is to bring this serious adverse event to the attention of appropriate healthcare workers.

Gastrointestinal obstruction caused by clozapine was reported in the UK 15 years ago and a warning added to the product information. In 1999 the Committee on Safety of Medicines published a short article on clozapine and gastrointestinal obstruction having received 20 spontaneous reports of clozapine-induced gastrointestinal hypomotility. A more recent review of 102 life threatening cases of clozapine-induced gastrointestinal hypomotility calculated the prevalence of this adverse effect to be 3 per 1000 patients exposed to clozapine. Risk factors included recent initiation of clozapine, high clozapine dose or serum level, concomitant anticholinergic use (eg tricyclic antidepressants, anti-Parkinsonian agents and other antipsychotics) or intercurrent illness.

Clozapine can have an adverse effect on the entire gastrointestinal tract, from oesophagus to rectum, and may cause bowel obstruction, ischemia, perforation, and aspiration of faeculent matter. The underlying mechanism is likely to be clozapine’s strong anticholinergic and antiserotonergic properties.

From the Chief Pharmaceutical Officer

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Although constipation may occur in up to 60% of patients treated with clozapine it is usually benign. The consequences of clozapine-induced hypomotility being unrecognised or undertreated and progressing to severe, even fatal, bowel obstruction are, however, probably under appreciated.

Health professionals should counsel patients about the risk of constipation with clozapine and question patients about their bowel movements. Patient education on healthy bowel habits and lifestyle may help, but for individuals without a structured routine and those not optimally controlled, monitoring for this adverse effect is essential. A patient prescribed clozapine, with or without a history of constipation, who presents with abdominal pain should be a cause for immediate concern and further investigation.


Professor Roger Walker
Chief Pharmaceutical Officer for Wales