The information in this document is not intended as a definitive treatment strategy, but as a suggested approach for clinicians. It is based on previous successful experience. Each case should, of course, be considered individually.

This information is provided for healthcare professionals and should not be used as a patient information leaflet.

SmPC statement
The Summary of Product Characteristics (SmPC) for Clozaril® (clozapine) states that:

Urinary incontinence and urinary retention are common (≥1/100 but <1/10) side-effects of Clozaril®. Nocturnal enuresis is also listed as an adverse effect which has a frequency of ‘not known’.

Background
Urinary incontinence is known to be associated with severe mental illness and neuroleptic medications, including clozapine. While not usually a health risk, it is a major negative influence on a patient’s quality of life and can lead to non-compliance. It may occur at any time during clozapine treatment, at any dose and is frequently nocturnal. It has been reported in males and females of all ages, although the elderly may be particularly susceptible. Childhood enuresis has been identified as a risk factor, as has severity of mental illness, constipation, sedation, diabetes and seizures.

The reported incidence in the literature ranges from around 2% up to around 40% (reported in one small case study evaluating 12 patients). There is evidence to suggest that it is often an under-reported side-effect due to the associated social stigma.

Urinary retention may be serious enough to require emergency treatment. Patients at most risk of developing retention are those with pre-existing conditions that involve incomplete voiding of the bladder, such as prostatic enlargement. Elderly patients are also particularly susceptible.

Mechanism
There are a number of possible mechanisms that can explain the occurrence of urinary retention and incontinence. The potent anticholinergic activity of clozapine may result in urinary retention with subsequent overflow resulting in incontinence.

It has also been proposed that the antiadrenergic activity of clozapine decreases bladder sphincter tone and causes bladder emptying. Urinary disorders may also occur as a secondary consequence of other disorders or side-effects associated with clozapine, for example, incontinence may be secondary to excessive sedation which then prevents the patient from waking during sleep to empty the bladder. Clozapine-induced constipation may aggravate urinary retention resulting in secondary overflow, and incontinence secondary to diabetes and seizures may also occur.
Prevention

It may be necessary to enquire specifically about incontinence since there is evidence to show that patients are reluctant to report what they see as an embarrassing side-effect.

Urinary incontinence often occurs at night (nocturnal enuresis) and it may be helpful to restrict fluids during the evening and make sure that patients urinate before going to bed. Patients should have easy access to a toilet and, in addition, it may be worth waking the patient during the night to use the toilet. Another consideration is to reduce the clozapine dose or alter the dosage schedule,\(^8\) reducing the evening dose to avoid deep sedation.

Due to the severity of urinary retention, it is recommended that elderly patients and those with prostatic enlargement or other pre-existing conditions that involve incomplete voiding of the bladder, are carefully supervised.\(^1,^2\) Constipation in patients on clozapine should be identified and managed due to the risk of developing gastrointestinal obstruction, in addition to the aggravation of retention.

Other drugs with anticholinergic or sedative side-effects should be avoided where possible.

Management

Urinary incontinence, as mentioned above, may be secondary to constipation, seizures or diabetes mellitus and it is important to distinguish and manage the underlying cause prior to initiating any treatment.

It is also important to ensure that urinary retention is excluded before treating the patient for urinary incontinence.

Some cases of urinary incontinence may resolve spontaneously.\(^3\)

For pharmacological treatment, please check local hospital trust guidelines on effective drug management of urinary incontinence.

Urinary retention should be managed in consultation with a urologist. Acute retention may require emergency catheterisation and hospital admission.

References