



Hey! How did the meeting with the big bosses go? ✓✓



Felt so calm. No excess baggage today 😊¹ ✓✓



MEET BELINDA: SALES REPRESENTATIVE



Describes her life as “spiralling out of control” almost every day for the last 6 months.

- Constantly worries that she will be late for appointments or that she may not finish her reports on time
 - Worries that her daughter may get seriously ill since she started attending day-care
 - Feels irritable, snapping at people for no reason
 - Complains of sweaty palms and rapid heartbeat
 - Often has muscle pain in her neck and shoulders
 - Finds it difficult to concentrate during team meetings
- Struggles to fall asleep at night even though she feels very tired
 - Is willing to consider pharmacotherapy for her anxiety if it does not impair her work performance or ability to drive to her appointments

Hypothetical case

GENERALISED ANXIETY DISORDER (GAD)^{1,2}

21 %

Occurs in up to
of adults in their lifetime¹



Twice as common in
women as it is in men²

**Considered to be a chronic illness with
fluctuating symptom severity²**

**Characterised by excessive
and persistent anxiety and
worry that²:**

- Is hard to control,
- Causes significant distress or impairment in social, occupational, or other important areas of functioning, and
- Occurs on more days than not for at least 6 months



Symptoms include²:

- Restlessness or feeling keyed up or on edge
- Being easily fatigued
- Difficulty concentrating or mind going blank
- Irritability
- Muscle tension
- Sleep disturbance (difficulty falling asleep or staying asleep; or restless, unsatisfying sleep)

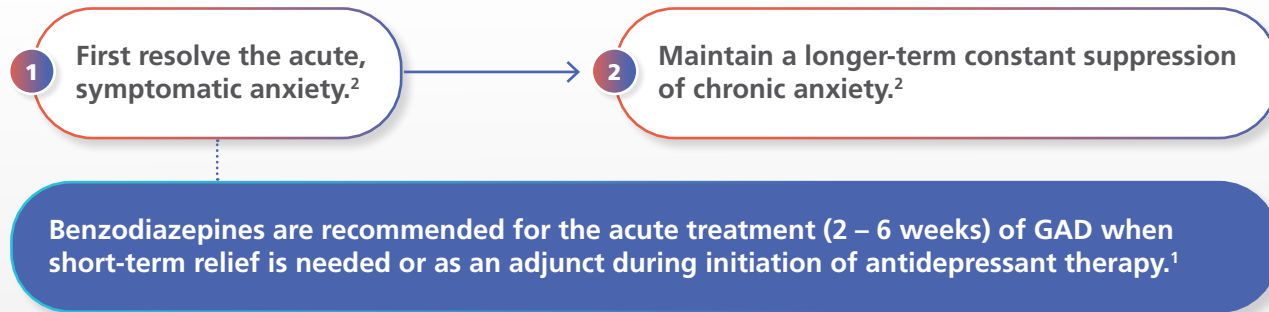
References: 1. Patriquin MA, Mathew SJ. The neurobiological mechanisms of generalized anxiety disorder and chronic stress. *Chronic Stress* 2017;1:1-10. 2. Baldwin D. Generalized anxiety disorder in adults: Epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis. 18 April 2022. UpToDate. Available online at <https://www.uptodate.com/contents/generalized-anxiety-disorder-in-adults-epidemiology-pathogenesis-clinical-manifestations-course-assessment-and-diagnosis>. [Accessed 28 November 2022].

GOALS OF TREATMENT FOR GAD¹



The long-term goal in GAD is to achieve and maintain remission.¹

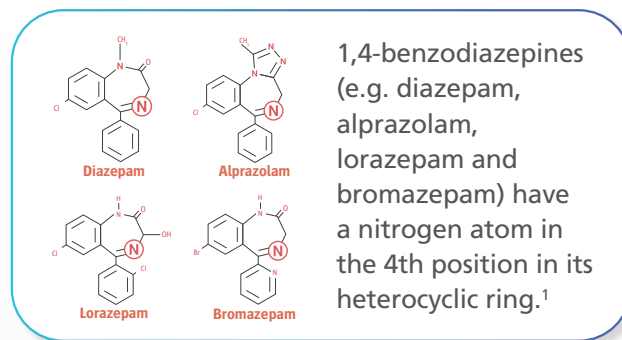
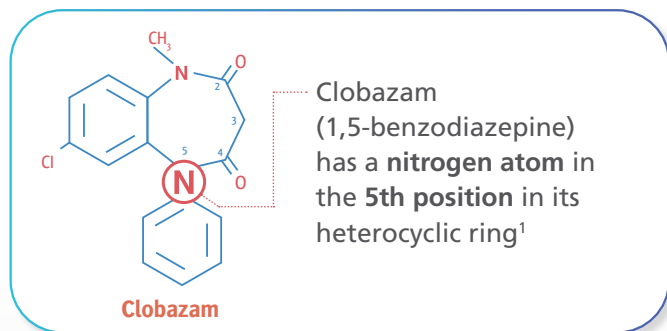
Treatment involves a sequential process²



GAD = Generalised anxiety disorder

References: 1. Botts S, Lockwood A, Allen T. Generalized anxiety disorder, panic disorder, and social anxiety disorder. Pharmacotherapy Principles and Practice. Second edition. Available online at <https://doctorlib.info/therapy/pharmacotherapy-principles-practice/43.html>. [Accessed 28 November 2022]. 2. Mandos LA, Reinhold JA, Rickels K. Achieving remission in generalized anxiety disorder. Psychiatr Times 2009;26(2). Available online at <https://www.psychiatrictimes.com/view/achieving-remission-generalized-anxiety-disorder>. [Accessed 28 November 2022].

CLOBAZAM E.G. URBANOL® IS CHEMICALLY AND STRUCTURALLY DIFFERENT FROM 1,4-BENZODIAZEPINES¹



Due to the structural difference, clobazam e.g. Urbanol® is a partial agonist to gamma-aminobutyric acid A (GABA_A) receptors (compared to 1,4-benzodiazepines, which are full agonists).²

Clobazam e.g. Urbanol®²:

- Has a lower affinity for the GABA_A ($\alpha_1\beta_2\gamma_2$) receptor, leading to fewer sedative side effects
- Has a selective agonist for GABA_A ($\alpha_2\beta_3\gamma_2$), thus exhibiting increased anxiolytic properties
- May have less effect on α_5 subunits resulting in a lesser effect on cognition

References: 1. Hindmarch I. Anxiety, performance and anti-anxiety drugs. Br J Clin Pract Suppl 1985;38:53-58. 2. Humayun MJ, Samanta D, Carson RP. Clobazam. Continuing Education Activity. 05 July 2020. National Center for Biotechnology Information (NCBI) Bookshelf. National Library of Medicine, National Institutes of Health. Available online at <https://www.ncbi.nlm.nih.gov/books/NBK541043/>. [Accessed 28 November 2022].

WHY THE HALF-LIVES OF BENZODIAZEPINES MATTER^{1,2,3}

Potent **benzodiazepines** that are **eliminated quickly** e.g. **lorazepam** (half-life: 10 - 18 hours) or **alprazolam** (half-life: 6 - 12 hours) **often lead to dependence and problems in withdrawal**¹

Clobazam e.g. Urbanol® has a mean half-life of 37,5 hours and is associated with **limited dependence and withdrawal symptoms following treatment**^{*2,3}



*In contrast to 1,4-benzodiazepines which can cause dependence, with sudden cessation of therapy resulting in withdrawal symptoms³

References: 1. Ashton CH. Guidelines for the rational use of benzodiazepines. Drugs 1994;48:25-40. 2. Sankar R. GABA_A receptor physiology and its relationship to the mechanism of action of the 1,5-benzodiazepine clobazam. CNS Drugs 2012;26:229-244. 3. Beaumont G. Clobazam in the treatment of anxiety. Hum Psychopharmacol 1995;10:S27-S41

IN SUMMARY

Clobazam e.g. **Urbanol®** provides **effective anxiolysis during and after treatment.*¹**

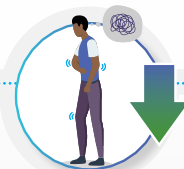


As effective as conventional anxiolytics during 4 weeks of treatment.*¹

Compared to 1,4-benzodiazepines, clobazam e.g. **Urbanol®** causes^{2,3:}



Less sedation
(Subjective)



**Less psychomotor and
cognitive impairment**



Less memory loss

*Daily doses: 30 mg clobazam; 15 mg diazepam; 3 mg lorazepam¹

The study authors reported no significant differences in anxiolytic efficacy between clobazam, lorazepam and diazepam during a 4-week treatment period. However, on cessation of therapy, there were significant differences between the groups in the maintenance of anxiolysis. The reduction in anxiety as assessed by a physician assessment scale was maintained in the clobazam group whereas in the other two treatment groups there was a significant deterioration in anxiety to pre-study levels.¹

Urbanol® is used in the treatment of anxiety in neurotic patients and for pre-operative medication. It may be effective in relieving the acute symptoms of the alcohol withdrawal syndrome but has no specific usefulness in the treatment of psychotic patients. Urbanol® is only indicated when the disorder is severe, disabling or subjecting the individual to extreme stress.⁴

References: 1. Beaumont G. Clobazam in the treatment of anxiety. Hum Psychopharmacol 1995;10:S27-S41. 2. Hindmarch I. Anxiety, performance and anti-anxiety drugs. Br J Clin Pract Suppl 1985;38:53-58. 3. Hindmarch I. The psychopharmacology of clobazam. Hum Psychopharmacol 1995;10:S15-S25. 4. Approved Urbanol® Professional Information. 27 September 2022.

DOSAGES AND DIRECTIONS FOR USE OF URBANOL®¹

- The normal adult dose ranges between 10 - 30 mg daily. Doses of 20 mg and above should preferably be given at bedtime or in divided doses.
- For elderly and debilitated patients as well as in children and clinically underweight patients, the daily dose should be halved.
- Treatment should be started with the lowest recommended dose. The maximum dose should not be exceeded.
- Treatment should be as short as possible. The patient should be reassessed after a period, not exceeding 4 weeks, and regularly thereafter in order to evaluate the need for continued treatment, especially where the patient is free of symptoms. The overall duration of treatment generally should not be more than 8 - 12 weeks, including a tapering off process.
- In certain cases, extension beyond the maximum treatment period may be necessary. If so, it should not take place without re-evaluation of the patient's status, using special expertise.
- It is strongly recommended that prolonged periods of uninterrupted treatment be avoided, since it may lead to dependence.



Reference: 1. Approved Urbanol® Professional Information. 27 September 2022.

For full prescribing information refer to the professional information approved by the Regulatory Authority.

SCHEDULING STATUS: [S5] **PROPRIETARY NAME AND DOSAGE FORM:** Urbanol® 5 mg capsules; Urbanol® 10 mg tablets. **COMPOSITION:** 5 mg or 10 mg clobazam. **REGISTRATION NUMBERS:** Urbanol® 5 mg: L/2.6/52; Urbanol® 10 mg: M/2.6/128. **NAMIBIA: SCHEDULING STATUS:** [NS3] **PROPRIETARY NAME AND DOSAGE FORM:** Urbanol® 5 mg capsules; Urbanol® 10 mg tablets. **COMPOSITION:** 5 mg or 10 mg clobazam. **REGISTRATION NUMBERS:** Urbanol® 5 mg: 90/2.6/001531; Urbanol® 10 mg: 90/2.6/001530. **NAME AND BUSINESS ADDRESS OF THE APPLICANT:** sanofi-aventis south africa (pty) Ltd., Reg. No.: 1996/10381/07. Floor 5, Building I, Hertford Office Park, 90 Bekker Road, Midrand, 2196. Telephone: + 27 11 256 3700. Facsimile: +27 11 256 3707. www.sanofi.com. For Medical Information Enquiries kindly contact ZA.Medinfo@sanofi.com. MAT-ZA-2200952-1.0-01/2023