IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Comparative Studies Between Clobazam And Carbamazepine

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1. Abstract

Epilepsy, including syndromes like Lennox-Gastaut syndrome (LGS), focal seizures, and generalized tonic-clonic seizures, requires tailored anticonvulsant therapies to optimize efficacy and minimize adverse effects. This comprehensive review compares clobazam, a 1,5-benzodiazepine that enhances GABAergic neurotransmission with reduced sedation **(Sankar, 2012; Gauthier & Mattson, 2015**), and carbamazepine, a sodium channel blocker effective for partial and tonic-clonic seizures but associated with enzyme induction and cutaneous risks **(French, 1994; Kehoe & Haw, 2020)**. Drawing from pharmacological, clinical, and neuropharmacological data, the analysis evaluates their physical and chemical properties, modes of action, advantages (e.g., clobazam's long-term efficacy in LGS; carbamazepine's versatility in neuropathic pain), disadvantages (e.g., clobazam's dependence risk; carbamazepine's hematologic toxicity), side effect profiles, toxicity (including teratogenicity), withdrawal symptoms, age-specific usage, and non-anticonvulsant applications (e.g., clobazam for anxiety; carbamazepine for bipolar disorder). Findings indicate clobazam offers a favorable safety profile for refractory pediatric epilepsy **(Klehm et al., 2014)**, while carbamazepine excels in focal seizures but demands monitoring for interactions **(Marson et al., 2002)**. Personalized treatment, considering patient age, seizure type, and comorbidities, is recommended to enhance quality of life and adherence **(Samanta, 2021; Strzelczyk & Schubert-Bast, 2022).** Future research should address gaps in long-term comparative trials.

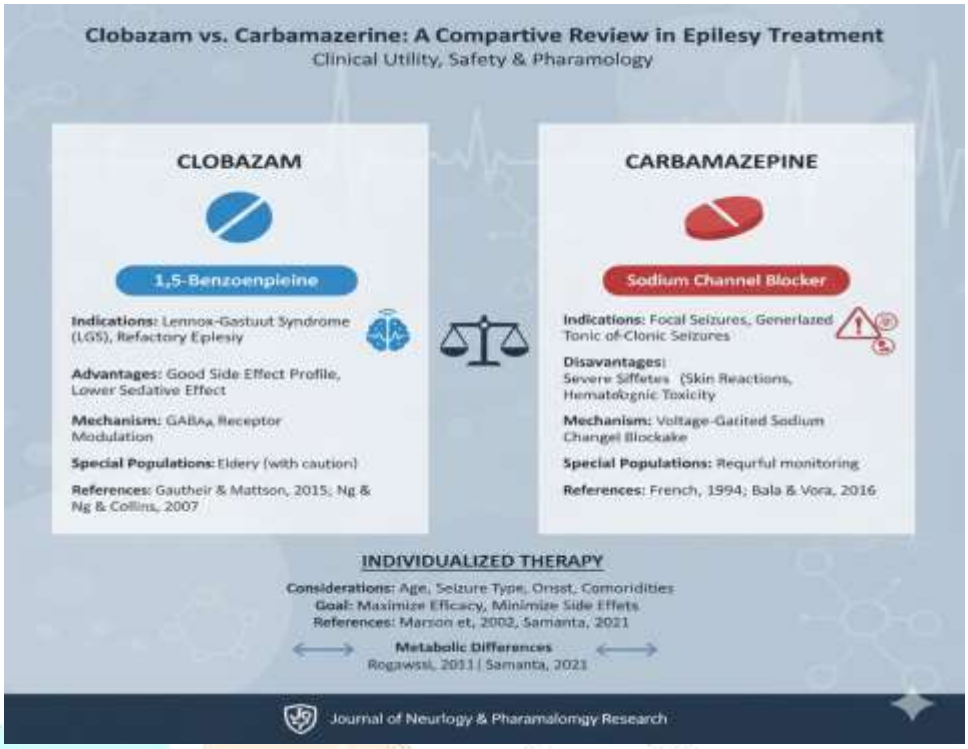


Figure 1. Comparative studies between Clobazam and Carbamazepine

Key points

Clobazam, Carbamazepine, Lennox-Gastaut syndrome, Focal seizures, Generalized Tonic-Clonic seizures, Side effect profile, Anticonvulsant therapy, Neuropharmacology.

2. Introduction

Many neurological disorders have been observed in humans for different reasons. One of them is Temporal Lobe Epilepsy (TLE), also known as Lennox-Gastaut Syndrome, which occurs in children. It is mainly associated with high morbidity and mortality **(Resnick & Sheth, 2017; Wheless & Constantinou, 1997)**. Several medicines and surgical processes are used to treat these disorders, among which this paper presents comparative studies on two medicines, Clobazam and Carbamazepine **(Samanta, 2021)**.

In the following papers, we will examine comparative studies between two widely used medications used to treat TLE. These papers give us detailed information on both medicines, their physical and chemical properties, mode of action, advantages and disadvantages, uses, toxicity to the human body, how one medicine differs from the other, and their pharmacological and pharmacodynamic effects on the human body **(Gauthier & Mattson, 2015; French, 1994)**.

Understanding how these drugs compare can help patients, caregivers, and healthcare providers make better treatment decisions for epilepsy and other related conditions. This review aims to highlight the key differences and similarities between clobazam and carbamazepine, focusing on their effectiveness, safety, and real-world usage **(Marson et al., 2002; Kehoe & Haw, 2020)**.

2.1. Significance

Comparing clobazam and carbamazepine is important for doctors and patients dealing with epilepsy and seizure disorders. These two drugs are common treatments, but they work in different ways and have a unique mode of action, side effects, and uses **(Sankar, 2012; Jo & Bean, 2014)**. Knowing how they stack up against each other helps doctors choose the best option, especially for children and adults with newly diagnosed or hard-to-treat epilepsy **(Klehm et al., 2014; Pellock, 1987)**. Research has shown that both drugs offer similar seizure control and similar long-term use rates after a year. However, they differ in the types of side effects they cause: carbamazepine tends to cause more physical side effects like skin rashes, while clobazam might cause more changes in behaviour **(Samanta, 2021; Bala & Vora, 2016)**. This information is key for creating personalised treatment plans, reducing unwanted effects, and helping patients feel better.

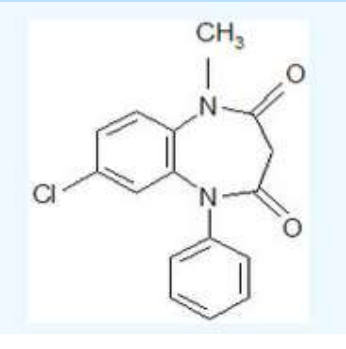
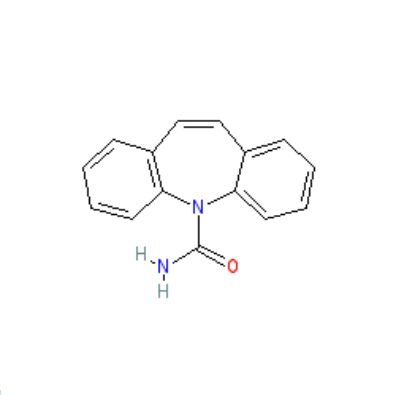
Since epilepsy often needs long-term treatment, knowing which drug is easier to tolerate or works faster can make a difference in how well patients stick to their medication and how well they do overall **(French, 1994; Gauthier & Mattson, 2015)**. Studies also show we need more options for treatment and better research to fill in the gaps we still have. This can help guide future studies and shape clinical guidelines.

2.2. Objective

The main goal of this review is to provide a detailed and evidence-based comparison of clobazam and carbamazepine for treating epilepsy. Specifically, it aims to:

- Evaluate how well clobazam and carbamazepine work when used alone or together with other medications for different types of epilepsy **(Marson et al., 2002; Montenegro et al., 2001).**
- Look at the safety and side effect profiles of both drugs, including how often and what kind of side effects they cause **(Kehoe & Haw, 2020; Pellock, 1987).**
- Review how long patients stay on these drugs, how quickly they control seizures, and how they affect quality of life **(Bawden et al., 1999; Klehm et al., 2014).**
- Identify which patients might do better with one drug or the other based on their health, the risk of side effects, or treatment goals **(French, 1994; Samanta, 2021).**

3. Overview of clobazam and carbamazepine

Overview of clobazam and carbamazepine		
	Clobazam	**Carbamazepine**
Structure		
Introduction	Clobazam is a type of medicine known as a benzodiazepine, often used to help control seizures, particularly in conditions like Lennox-Gastaut syndrome. It works by enhancing the calming effects of a brain chemical called GABA, which helps reduce the likelihood of experiencing a seizure **(Sankar, 2012; Gauthier & Mattson, 2015)**. Compared to older benzodiazepines, Clobazam generally causes less drowsiness **(Hindmarch, 1979)**. It is typically provided as an additional treatment for epilepsy in children aged two and older. While taking Clobazam, some individuals may experience sleepiness or constipation, so it is important to use it carefully and under the supervision of a doctor to avoid the risk of dependence on it **(Ng & Collins, 2007; Klehm et al., 2014)**.	Carbamazepine is a common anticonvulsant drug, although it is primarily used for controlling epilepsy, specifically partial and generalized Tonic-Clonic seizures, and for certain pain, like trigeminal neuralgia, and certain mood disturbances like bipolar disorder **(French, 1994; Okuma & Kishimoto, 1998; Motika & Smith, 2010)**. Its therapeutic impact is largely due to preventing voltage-gated sodium channel openings, thus decreasing excessive neuronal discharge and stabilizing nerve conduction **(Jo & Bean, 2014)**. Carbamazepine has been a cornerstone drug for epilepsy, distinguished by efficacy, yet requiring close monitoring due to a relatively narrow therapeutic index, drug interaction potential, and risk for adverse reaction, most notably rare yet severe cutaneous reactions in subjects with a genetic predisposition **(Kehoe & Haw, 2020; Bala & Vora, 2016)**.
History	Clobazam, a 1,5-benzodiazepine, was first synthesized in 1966 and published in 1969. It was initially developed as an anxiolytic (anti-anxiety medication) and was approved in Australia (1970) and France (1974) for that purpose. Marketing for epilepsy began in 1984. In 2005, it was approved in Canada as an add-on therapy for various seizure types. In the US, the FDA	Carbamazepine was discovered by chemist Walter Schindler at J.R. Geigy AG (now part of Novartis) in Basel, Switzerland, in 1953. Carbamazepine has been a cornerstone drug for epilepsy since the 1960s. It was first marketed as a drug to treat epilepsy in Switzerland in 1963 under the brand name Tegretol; its use for trigeminal neuralgia (formerly known as tic douloureux) was introduced at the same time. It has been

	approved clobazam in 2011 for Lennox-Gastaut syndrome (LGS) in individuals two years or older **(Ng & Collins, 2007; Gauthier & Mattson, 2015)**.	used as an anticonvulsant and antiepileptic in the United Kingdom since 1965 and has been approved in the United States since 1968. Carbamazepine was studied for bipolar disorder throughout the 1970s **(Schindler, 1960; Okuma & Kishimoto, 1998; Motika & Smith, 2010)**.
Approval	It was approved in Australia (in 1970) and France (in 1974) for anxiety. Marketing for epilepsy began in 1984 **(Gauthier & Mattson, 2015).**	Carbamazepine was first marketed in 1962 and approved in the United States for trigeminal neuralgia in 1968 **(Motika & Smith, 2010)**.
Role in epilepsy treatment	Clobazam is incorporated into a treatment regimen for epilepsy, specifically targeting seizures associated with Lennox-Gastaut syndrome (LGS). It prevents seizures by acting on the brain. Clobazam belongs to a class of medications known as benzodiazepines, which function by enhancing a calming neurotransmitter in the brain known as GABA **(Sankar, 2012; Gauthier & Mattson, 2015)**.	Carbamazepine is used to manage and treat epilepsy, trigeminal neuralgia, and acute manic and mixed episodes in bipolar disorder. Indications for epilepsy are specifically for partial seizures with complex symptomatology (psychomotor, temporal lobe), generalized tonic seizures (grand mal), and mixed seizure patterns **(French, 1994; Marson et al., 2002)**.

Table: -1 – Overview of clobazam and carbamazepine

4. Physical and Chemical properties

Physical Properties			Chemical Properties		
	Clobazam	**Carbamazepine**		**Clobazam**	**Carbamazepine**
Molecular formula	C16H13ClN2O2 **(University of Alberta; Drug Bank, 2025).**	C15H12N2O **(University of Alberta; Drug Bank, 2025)**	**IUPAC name**	7-chloro-1-methyl-5-phenyl-1,5-benzodiazepin-2,4-dione **(University of Alberta; Drug Bank, 2025)**	5H-dibenz [b, f] azepine-5-carboxamide **(University of Alberta; Drug Bank, 2025)**
Molecular weight	300.74 g/mol **(University of Alberta; Drug Bank, 2025)**	236.27 g/mol **(University of Alberta; Drug Bank, 2025)**	**Chemical Class**	1,5-Benzodiazepine **(Gauthier & Mattson, 2015)**	dibenzoazepine, specifically an imino stilbene derivative, and is structurally related to tricyclic antidepressants **(Gauthier & Mattson, 2015)**
Boiling point	It decomposes before reaching its boiling point. **(University of Alberta; Drug Bank, 2025)**	399.6±45. **(University of Alberta; Drug Bank, 2025)**	**Hydrophobicity**	Lipophilic **(University of Alberta; Drug Bank, 2025)**	Carbamazepine is moderately hydrophobic with a log P value between 2.1 and 2.77, indicating good lipid solubility but poor water solubility **(University of Alberta; Drug Bank, 2025).**
Melting Point	182-185ºC **(University of Alberta; Drug Bank, 2025)**	189-192 **(University of Alberta; Drug Bank, 2025)**	**Ionization**	Weakly basic with a pKa of ~4.4. Ionizes in acidic environments (e.g., stomach) **(University of Alberta; Drug Bank, 2025)**	remains largely unionized in the body **(University of Alberta; Drug Bank, 2025)**

Solubility	Slightly soluble in water, sparingly soluble in ethanol, freely soluble in methylene chloride. **(University of Alberta; Drug Bank, 2025)**	Soluble in alcohol, acetone and propylene glycol; practically insoluble in water. **(University of Alberta; Drug bank, 2025)**	**Stereochemistry**	Chiral Centre at the 5-position (racemic mixture in clinical formulations) . **(University of Alberta; Drug Bank, 2025)**	Carbamazepine is an achiral molecule; it does not possess stereocenters and exists as a single, non-chiral form **(University of Alberta; Drug Bank, 2025)**
Physical appearance	white to off-white crystalline powder **(University of Alberta; Drug Bank, 2025)**.	White to off-white crystalline powder **(University of Alberta; Drug Bank, 2025)**.	**Hydrogen Bonding**	Contains two ketone oxygen atoms and one tertiary amine nitrogen, acting as hydrogen bond acceptors **(University of Alberta; Drug Bank, 2025)**	It has one hydrogen bond donor (the amide NH) and one hydrogen bond acceptor (the carbonyl oxygen) **(University of Alberta; Drug Bank, 2025)**
XLogP3 value	2.1 **(University of Alberta; Drug Bank, 2025)**	2.5 **(University of Alberta; Drug Bank, 2025)**	**Polarity**	Low polarity due to aromatic rings and chlorine substituent **(University of Alberta; Drug Bank, 2025)**	Carbamazepine has low polarity, reflected by a topological polar surface area of about 46.33 Å². Its aromatic rings and limited polar groups contribute to its overall non-polar character **(University of Alberta; Drug Bank, 2025)**.
Taste and odour	Slightly bitter taste **(University of Alberta; Drug Bank, 2025)**	White to off-white powder **(University of Alberta; Drug Bank, 2025)**	**Chemical Stability**	Stable in crystalline form- P. Degrades under strong acidic/basic conditions or	Carbamazepine is chemically stable under standard storage conditions, but may degrade

				prolonged UV exposure. **(University of Alberta; Drug Bank, 2025)**	under extreme heat or light. **(University of Alberta; Drug Bank, 2025)**
			Reactivity	Undergoes hepatic metabolism via CYP enzymes **(Huddart et al., 2018).**	Relatively non-reactive under physiological conditions, but can undergo metabolic oxidation in the liver **(Tolou-Ghamari et al., 2013; Jo & Bean, 2014).**
			Metabolism	**Primary Pathway**: *N*-demethylation by CYP3A4 to active metabolite *N*-desmethylclobazam (Nor-clobazam). **Secondary Pathway**: Hydroxylation by CYP2C19 to 4′-hydroxyclobazam (minor metabolite). **Excretion**: <3% excreted unchanged; metabolites eliminated via urine (hydroxylated forms). **Genetic Impact**: CYP2C19 poor metabolizers	Carbamazepine is metabolized mainly in the liver by the CYP3A4 enzyme to its active metabolite, the carbamazepine-10,11-epoxide. This latter compound is, in turn, inactivated by the epoxide hydrolase of the microsomal system to form the carbamazepine-trans-10,11-diol and secondary metabolites, which are excreted predominantly in the urine. Carbamazepine is a powerful inducer of the hepatic enzymes, and this can influence its rate **(Tolou-Ghamari et al.,**

				show elevated Nor-clobazam levels, requiring dose adjustments. **(Huddart et al., 2018).**	**2013; Jo & Bean, 2014).**

Table: - 2- physical and chemical properties of clobazam and carbamazepine

5. Mode of Action

5.1. Mode of Action of Clobazam

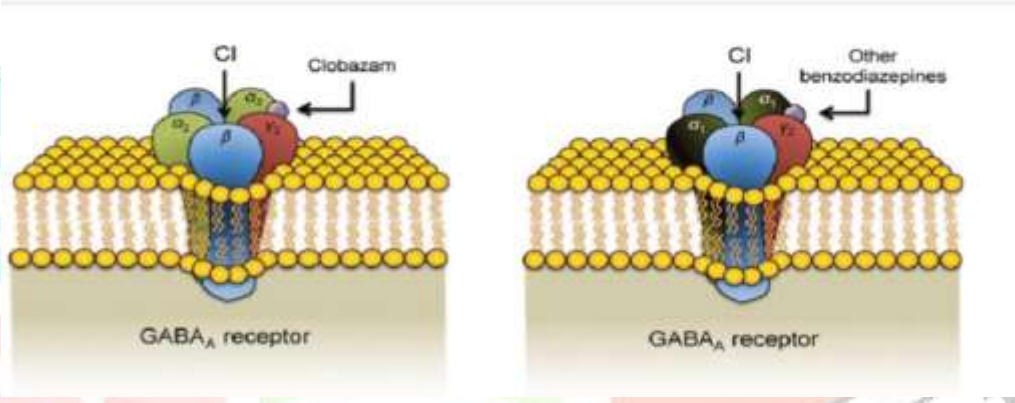


Figure 2: Mode of Action of clobazam VS other Benzodiazepines on GABA Receptor

Clobazam is a 1,5-benzodiazepine, fundamentally disconnected from classical benzodiazepines and, thus, a fractional agonist at the GABA-A receptors. Not at all like full agonist BZDs, clobazam shows less authoritative to the α1β2γ2 (BZ-1) receptor, resulting in less narcotic impacts, and it transcendently ties to the α2β3γ2 receptor, which accounts for its expanded anxiolytic and anticonvulsant impacts. It upgrades GABAergic neurotransmission at the GABA-A receptor benzodiazepine official location, which improves the conductance of chloride particles, causing hyperpolarization and restraint of neuronal termination **(Sankar, 2012; Gauthier & Mattson, 2015)**. Particular official of clobazam to the α2 subunit relative to the α1 subunit diminishes its narcotic impacts in comparison with 1,4-benzodiazepines and may diminish the potential for resistance **(Ng & Collins, 2007)**. The GABA-A receptor contains five subunits, two α, two β and one γ, and clobazam ties to the interface between the α and the γ2 subunit, which leads to the next rate of the chloride channel opening, resulting in increased hyperpolarization **(Sankar, 2012)**. Advance, clobazam increases GABA transporter 3 expression, which may support its wide anticonvulsant or anxiolytic range, with fewer cognitive side effects than on account of its lesser impact on α5 subunits **(Huddart et al., 2018)**.

5.2. Mode of Action of Carbamazepine

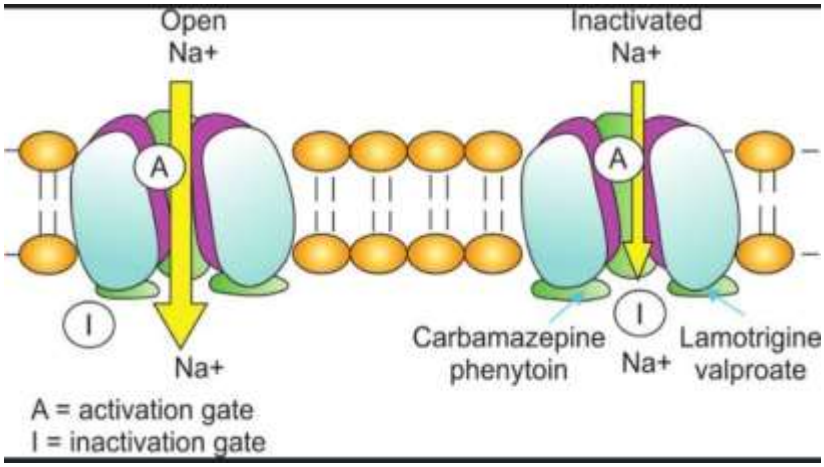


Figure 3: Mode of action of Carbamazepine

Epilepsy happens when there's too much sodium surging into brain cells and a balance between calming and strengthening neurotransmitters. Sodium channels help make these signals. Carbamazepine controls this by inhibiting how quickly these channels can reactivate, lessening fast and rehashed wrapping up of signals. Carbamazepine also boosts the calming neurotransmitter GABA and brings down the excitatory one, glutamate **(Motika & Smith, 2010; Liu et al., 2006)**. It influences how sodium, potassium, and calcium move in and out of cells, and additionally impacts neurotransmitters that trigger seizures. At higher measurements, carbamazepine can inhibit the reuptake of catecholamines and other biogenic amines since it's chemically similar to tricyclic antidepressants. It can moreover relate to adenosine receptors (A1 and A2), redesigning adenosine's calming impacts. But it can moreover act against adenosine receptors, which might increase nerve enhancement **(Jo & Bean, 2014; French, 1994)**. Long-term utilize can make cells less sensitive to the drug by creating receptor sites. Carbamazepine also impacts serotonin, in shows up, although it's foggy how this makes a difference with seizures. It may release serotonin and in truth piece its reuptake. It can affect other types of calcium channels, reducing how much neurotransmitter is discharged. Later examination in animal models shows that carbamazepine can specifically and that make certain types of seizures more detestable, like absence seizures, by interferometer with GABAergic signalling in specific brain regions **(Liu et al., 2006)**. Generally, carbamazepine is, on an essential level, a sodium channel blocker that calms down overactive brain signals. In bipolar disorder, it may offer help in development by boosting GABA and dopamine levels. Be that as it may, around 30% of patients develop resistance to carbamazepine, which would be due to changes in how their bodies handle the drug (including the EPHX1 gene promoter) **(Tolou-Ghamari et al., 2013; Kehoe & Haw, 2020)**.

6. Advantages, Disadvantages, as well as uses of clobazam and carbamazepine

6.1. Advantages and Disadvantages

Advantages		Disadvantages	
Clobazam	**Carbamazepine**	**Clobazam**	**Carbamazepine**
Effective Seizure Control: - 50% of patients can achieve at least a 50% reduction in seizure frequency, with some achieving complete seizure control **(Montenegro et al., 2001; Klehm et al., 2014)**.	**Broad Anticonvulsant Efficacy:** - carbamazepine has shown efficacy in treating mixed seizures, partial seizures with complex symptoms, and generalized Tonic-Clonic seizures. It is used off-label as a second-line treatment for bipolar disorder **(Motika & Smith, 2010; French, 1994).**	**Risk of Dependence and Withdrawal:** - Abrupt discontinuation can lead to severe withdrawal symptoms, including anxiety, insomnia, tremors, hallucinations, and even seizures, which may be life-threatening if not medically supervised. Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death **(Lafleur, 2016; Rickels et al., 1990).**	**Severe Cutaneous Reactions** Stevens–Johnson Syndrome is a rare side effect of carbamazepine. It causes flu-like symptoms, followed by a red or purple rash that spreads and forms blisters. The affected skin eventually dies and peels off **(Bala & Vora, 2016; Kehoe & Haw, 2020).**
Favourable Safety Profile: - It has demonstrated great efficacy and a high safety profile in refractory epilepsy and a few monotherapy trials in both children and adults **(Gauthier & Mattson, 2015)**.	**Proven Effectiveness for Neuropathic Pain:** - It is the only FDA-approved medication for trigeminal neuralgia and is widely used to manage other neuropathic pain syndromes, providing significant pain relief where other treatments may fail **(Porter, 2008).**	**Potential for Abuse and Misuse:** - Misuse of Clobazam can lead to overdose, profound sedation, respiratory depression, coma, or death, especially if combined with other central nervous system depressants such as opioids **(Schweizer et al., 1991).**	**Hematologic Toxicity:** - Carbamazepine can cause blood disorders, such as agranulocytosis, aplastic anaemia, low platelet levels (thrombocytopenia), and low white blood cell levels (leukopenia) **(Pellock, 1987; Crepeau et al., 2012).**
Less Sedation: - It causes less sedation than other 1,4-benzodiazepines.	**Mood Stabilization in Bipolar Disorder:** - Carbamazepine is	**Sedation and Cognitive Impairment:** - Many patients have	**Hepatotoxicity:** - This medicine may cause a condition called drug reaction

For example, healthy volunteers who took clobazam at 10 or 20 mg/day experienced fewer psychomotor and sedation side effects than those who took clonazepam at 0.5 and 1 mg/day **(Hindmarch, 1979)**.	effective in treating acute manic and mixed episodes in bipolar I disorder, offering an alternative to lithium or valproate for mood stabilization **(Okuma & Kishimoto, 1998).**	signs and symptoms of respiratory depression and sedation. These effects are dose-dependent and may impair daily functioning, especially at treatment initiation or with dose increases **(Bawden et al., 1999; Besag & Vasey, 2021).**	with eosinophilia and systemic symptoms (DRESS), which is a serious allergic reaction affecting multiple body organs (e.g., liver or kidney). Check symptoms like fever, dark urine, headache, rash, stomach pain, swollen, painful, or tender lymph glands in the neck, armpit, or groin, unusual tiredness, or yellow eyes or skin. **(Smith et al., 2022).**
Long-Term Efficacy: - most patients who initially respond to clobazam continue to benefit for years without needing significant dose increases **(Ng & Collins, 2007)**.	**Long Track Record and Extensive Clinical Experience: -**With decades of use, carbamazepine's safety and efficacy profiles are well established, allowing clinicians to rely on a wealth of data for dosing, monitoring, and managing side effects **(Kehoe & Haw, 2020).**	**Behavioural and Mood Changes: -** It may cause irritability, aggression, agitation, restlessness, mood swings, and, in rare cases, confusion or hallucinations **(Strzelczyk & Schubert-Bast, 2022).**	**Drug Interactions via CYP3A4 Induction: -** Carbamazepine strongly induces CYP3A4, reducing efficacy of oral contraceptives, warfarin, and many antipsychotics. Dose adjustments for co-administered drugs are often necessary **(Kehoe & Haw, 2020).**
Adjunctive and Monotherapy Use: - Clobazam can be used both as an add-on therapy for refractory epilepsy and, in some cases, as monotherapy. Its flexibility allows it to be tailored to individual patient needs **(Canadian Clobazam Cooperative Group, 1991)**.	**Availability in Multiple Formulations: -** Carbamazepine is available in various oral forms (tablets, chewable tablets, extended-release tablets/capsules, and oral suspension), enabling flexible dosing for different patient needs and age groups **(FDA,**	**Motor Coordination and Speech Disturbances: -** Patients may experience unsteady gait, tremors, slurred speech, and other motor function problems **(Meador et al., 2007).**	**Narrow Therapeutic Index: -** Therapeutic drug monitoring is critical due to a narrow window (4–12 µg/mL). Toxicity (e.g., seizures, coma) occurs at levels >20 µg/mL, requiring careful titration **(French, 1994).**

	2025; Wikipedia, 2025).		
Anxiolytic Benefits: - In addition to its anticonvulsant effects, clobazam also reduces anxiety, which is particularly helpful for epilepsy patients **(Brogden et al., 1980; DeVane, 2016).**	**Cost-Effectiveness:** -As a generic medication, carbamazepine is widely accessible and affordable, making it a practical choice for long-term management of chronic neurological and psychiatric **conditions (Marson et al., 2002).**	**Rare but Serious Adverse Reactions:** - severe skin reactions such as Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) **(Bala & Vora, 2016).**	**Paradoxical Seizure Aggravation:** - Carbamazepine may also be used to treat mixed seizure types or other types of partial or generalized seizures; however, it appears ineffective for absence seizures **(Liu et al., 2006).**
Superior Efficacy in Certain Syndromes: - In head-to-head studies, high-dose clobazam was found to be superior to rufinamide, felbamate, lamotrigine, and topiramate in reducing drop seizures in Lennox–Gastaut syndrome, and it provided a greater median reduction in total seizure frequency **(Ng & Collins, 2007; Gauthier & Mattson, 2015).**	**Efficacy Comparable to Other First-Line Antiepileptic Drugs:** -Clinical trials and meta-analyses show that carbamazepine is as effective as phenytoin and valproate for focal and generalized tonic-clonic seizures, supporting its continued use as a standard therapy **(Marson et al., 2002).**	**Gastrointestinal and Autonomic Side Effects:** - It includes decreased appetite, constipation, drooling, vomiting, and other gastrointestinal symptoms **(Crepeau et al., 2012).**	**Neuropsychiatric Side Effects** disturbances: -Very common: Dizziness (44%), somnolence (32%), ataxia (15%) Common: Headache, tremor Uncommon: tremor, asterixis, dystonia, tics Rare: Choreoathetotic disorders **(Kehoe & Haw, 2020; Aldenkamp et al., 1987)**, orofacial dyskinesia, oculomotor disturbances, speech disorders, peripheral neuritis, paraesthesia, paretic symptoms, neuroleptic malignant syndrome Frequency not reported: Drowsiness, fatigue, taste

Improved Quality of Life: - By effectively controlling seizures and reducing anxiety, clobazam helps improve the overall quality of life for patients with epilepsy **(Klehm et al., 2014).**	**Versatility in Treating Multiple Conditions:** - beyond epilepsy, carbamazepine is used off-label for alcohol withdrawal syndrome, restless leg syndrome, and certain types of tinnitus, demonstrating its therapeutic versatility **(Barrons & Roberts, 2010; Aurora et al., 2012).**	**Contraindications and Cautions in Special Populations:** - Clobazam should be used with caution in patients with liver impairment, respiratory problems, myasthenia gravis, or a history of drug or alcohol dependence. It is also not recommended during pregnancy due to the potential risks of birth defects and neonatal withdrawal **(Nucera et al., 2022).**	**Overdose Risks: -** CBZ has a molecular weight of 236 and sticks tightly to proteins in the blood (around 70%-80%). Because it's very fatty (lipophilic), it spreads quickly through the body, with a volume of distribution of about 0.8 to 1.4 liters per kilogram. In normal doses, it reaches its highest blood levels in 6-8 hours (immediate-release tablets) or 12-24 hours (controlled-release). But if someone takes too much, it can take much longer—up to 106 hours—because it slows down the gut, delaying how quickly it's absorbed **(Alrashood, 2016)**.

Table: -3- Advantages and Disadvantages of Clobazam and Carbamazepine

6.2. Uses

6.2.1. Clobazam

I. Adjunctive Treatment of Lennox-Gastaut Syndrome (LGS) **(Ng & Collins, 2007; Gauthier & Mattson, 2015).**

II. Drug–Resistant Focal Seizure **(Canadian Clobazam Cooperative Group, 1991).**

III. Dravet Syndrome Management **(Arya et al., 2018).**

IV. Generalized Tonic–Clonic Seizure **(Gauthier & Mattson, 2015).**

V. Childhood Epilepsy Syndrome **(Klehm et al., 2014; Bawden et al., 1999).**

VI. Acute seizure Control **(Shimizu et al., 2003).**

VII. Transition Therapy During Medication Adjustment **(Humayun, Samanta, & Carson, 2020).**

VIII. Myoclonic seizure In Juvenile Myoclonic Seizure **(Arya et al., 2018).**

IX. Elderly Patients with Comorbid Anxiety **(Brogden, Heel, Speight, & Avery, 1980).**

X. Reducing Polypharmacy Burden **(Smith et al., 2022).**

6.2.2. Carbamazepine

I. First-Line Treatment for Focal (Partial) Seizures **(Motika & Smith, 2010).**
II. Management of Generalized Tonic-Clonic Seizures **(Marson et al., 2002)**.
III. Mixed Seizure Patterns **(Cereghino et al., 1975)**.
IV. Prevention of Seizure Recurrence **(Callaghan & Goggin, 1988).**
V. Long-Term Maintenance Therapy **(French, 1994)**
VI. Adjunctive Therapy in Drug-Resistant Epilepsy **(Cereghino et al., 1975).**
VII. Pediatric Use in Partial and Generalized Seizures **(Pellock, 1987).**
VIII. Post-Traumatic Epilepsy **(Agrawal, Timothy, Pandit, & Manju, 2006).**
IX. Prevention of Secondary Generalization **(Glötzner et al., 1983).**
X. Reduction of Seizure Frequency and Severity **(Marson et al., 2002).**

7. Side Effects and Toxicity of Clobazam and Carbamazepine

7.1. Side effects

Clobazam	Carbamazepine
Sedation, drowsiness **(Gauthier & Mattson, 2015; Bawden et al., 1999).**	Drowsiness, dizziness **(Pellock, 1987; Kehoe & Haw, 2020).**
Dizziness, lightheadedness **(Bawden et al., 1999).**	Ataxia (poor coordination) **(French, 1994)**
Ataxia (unsteady movements) **(Gauthier & Mattson, 2015).**	Diplopia (double vision) **(Pellock, 1987).**
Cognitive impairment (memory, concentration) **(Bawden et al., 1999).**	Nausea, vomiting, and GI upset **(Pellock, 1987).**
Muscle weakness **(Gauthier & Mattson, 2015)**	Rash (including severe skin reactions like Stevens-Johnson syndrome or TEN) **(Sangineedi et al., 2025; Bala & Vora, 2016).**
Fatigue **(Bawden et al., 1999)**	Blood cell changes (anaemia, leukopenia, thrombocytopenia) **(Kehoe & Haw, 2020)**
Double vision (diplopia, less common)	Liver enzyme elevation, hepatotoxicity **(Kehoe & Haw, 2020)**
Respiratory depression (high doses or overdose) **(Rickels et al., 1990; Brogden et al., 1980; Gauthier & Mattson, 2015).**	Hyponatremia (low sodium**) (Kehoe & Haw, 2020)**
Dependence and withdrawal symptoms (with long-term use) **(Lafleur, 2016).**	Allergic reactions (rash, rarely anaphylaxis) **(Bala & Vora, 2016)**
Behavioral changes (irritability, aggression) **(Gauthier & Mattson, 2015).**	Blurred vision **(Pellock, 1987; Kehoe & Haw, 2020).**

Nausea and constipation **(Crepeau et al., 2012)**	Tremor **(Kehoe & Haw, 2020)**
Allergic reactions (including rare facial swelling/angioedema) **(Gauthier & Mattson, 2015)**	Behavioral changes (mood swings, irritability) **(French, 1994)**
Suicidal thoughts **(Gauthier & Mattson, 2015)**	Suicidal thoughts **(Kehoe & Haw, 2020)**

Table: - 4- Side effects of neurological drug

7.2. Toxicity

7.2.1. Pregnancy consideration and teratogenicity

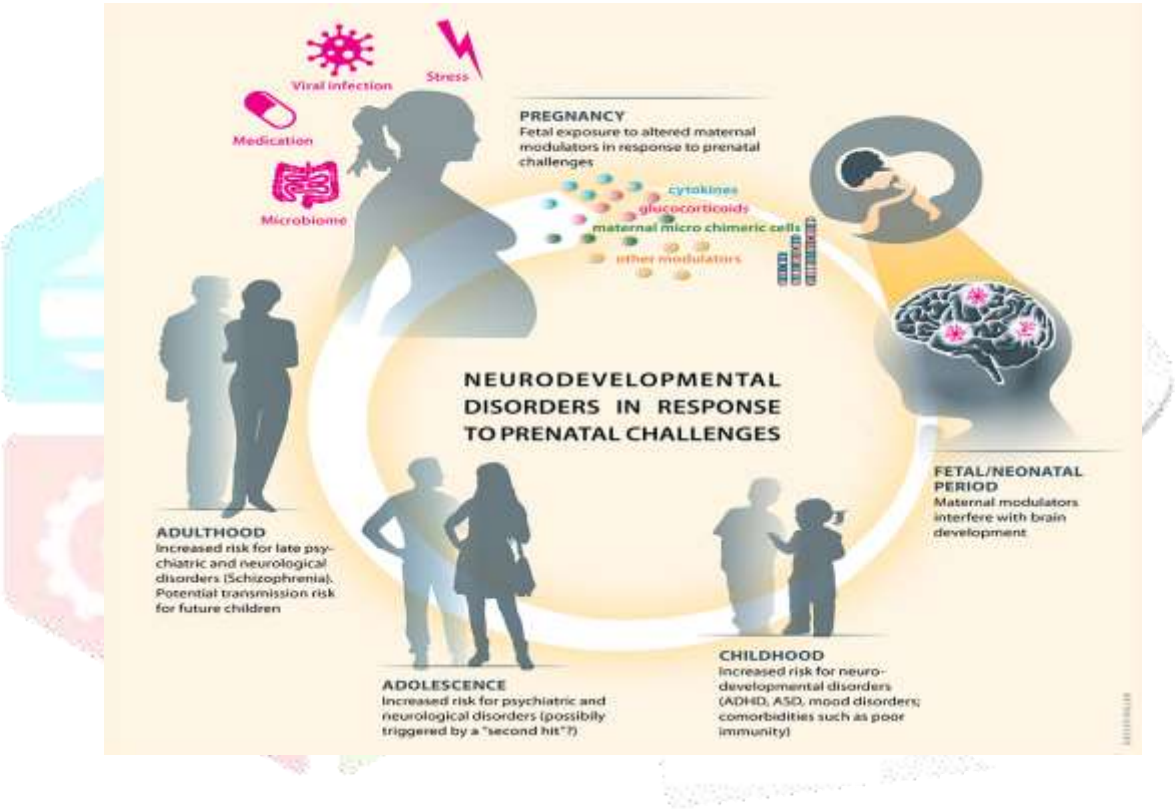


Figure 4: Toxicity of neurological drugs during Pregnancy consideration

Clobazam and carbamazepine pose specific threats during pregnancy. Clobazam, a benzodiazepine, is associated with a 22.2% rate of major inherent changes (MCMs) in small human contemplations, including neural tube and cardiac absconds, although genuine significance remains questionable **(Hoeltzenbein et al., 2023)**. Animals consider almost interfacing it to cleft sense of taste and embryofetal mortality at subtherapeutic measurements **(Besag & Vasey, 2021)**. Neonatal dangers include withdrawal side effects and floppy newborn child clutter, especially with third-trimester presentation **(Crepeau et al., 2012; Nucera et al., 2022)**. Clobazam is contraindicated during the to start with trimester and breastfeeding due to sedation threats division **(Gauthier & Mattson, 2015)**, carbamazepine shows well-documented teratogenicity, with a 3.3% MCM rate (spina bifida, cardiovascular absconds) and extended threats of microcephaly or moo gestational age **(Matalon et al., 2002; El-Gaafarawi & Abouel-Magd, 2015)**. A 2025 overview highlighted its collusion with enhancement hindrances, requiring fetal recognition and high-dose folic damaging supplementation **(Hoeltzenbein et al., 2023; Nucera et al., 2022).**

Both drugs require an exacting risk-benefit investigation. Carbamazepine's enzyme-inducing properties complicate polytherapy **(Kehoe & Haw, 2020)**, whereas clobazam's higher MCM flag in restricted information warrants caution **(Gauthier & Mattson, 2015)**. Carbamazepine is contraindicated in non-epileptic seizures due to seizure exacerbation **(Liu et al., 2006)**, though clobazam's utilization is confined to headstrong cases **(Samanta, 2021).** Clinically, carbamazepine's teratogenic profile is more established **(Matalon et al., 2002)**, but clobazam's neonatal withdrawal and sedation dangers require a rise in carefulness **(Crepeau et al., 2012).** Options like lamotrigine are favoured when attainable, emphasizing personalized care in pre-birth epilepsy administration **(Nucera et al., 2022).**

7.2.2. Neurocognitive effects

When it comes to how these medicines affect thinking and memory, clobazam and carbamazepine show some differences, but overall, both are considered to have a mild impact for most people. Studies have found that clobazam generally causes little to no trouble with memory, attention, or learning, and some children even show improvements in alertness and focus while taking it **(Bawden et al., 1999; Klehm et al., 2014)**. Most individuals taking clobazam don't report major issues with considering, and any side effects are usually mild and tolerable **(Strzelczyk & Schubert-Bast, 2022; Aldenkamp et al., 1987).**

Carbamazepine, on the other hand, has been linked to mild slowing in information processing, attention, and sometimes memory, especially at higher doses or with long-term use **(Meador et al., 2007; Wesnes et al., 2009)**. A few individuals may take note they are a bit slower to respond, have difficulty with word finding, or feel less sharp, but these impacts are ordinarily not serious and can move forward on the off chance that the estimations is reduced or the medication is stopped **(Kehoe & Haw, 2020; French, 1994).** In general, both medicines are much better for thinking and memory than older drugs like phenobarbital, but clobazam may have a slight edge in causing fewer cognitive side effects for most patients **(Gauthier & Mattson, 2015; Bawden et al., 1999**).

8. Withdrawal Symptoms of Clobazam VS Carbamazepine

Clobazam	Carbamazepine
Anxiety and irritability **(Humayun et al., 2020; Brogden et al., 1980)**	Seizures **(Kehoe & Haw, 2020; Pellock, 1987; Gayford & Redpath, 1969)**
Insomnia **(Humayun et al., 2020; Brogden et al., 1980)**	Headache **(Kehoe & Haw, 2020; Pellock, 1987)**
Tremors **(Humayun et al., 2020; Brogden et al., 1980)**	Nausea and vomiting **(Pellock, 1987; Gayford & Redpath, 1969)**
Sweating **(Humayun et al., 2020; Brogden et al., 1980)**	Anxiety and irritability **(Schweizer et al., 1991; Ries et al., 1989)**
Seizures**(Humayun et al., 2020; Brogden et al., 1980)**	Insomnia **(Schweizer et al., 1991; Ries et al., 1989)**
Agitation **(Humayun et al., 2020; Brogden et al., 1980)**	Dizziness and imbalance **(Kehoe & Haw, 2020; Pellock, 1987)**
Nausea and vomiting **(Humayun et al., 2020; Brogden et al., 1980)**	Muscle aches and pains **(Schweizer et al., 1991; Ries et al., 1989)**

Table: - 5 – Withdrawal Symptoms of Neurological Drugs

9. In different age groups (children VS adults)

9.1. Usage of clobazam in different age groups

	Children	Adult
Indication	Used specifically in the case of Lennox-Gastaut syndrome and refractory cases **(Resnick & Sheth, 2017; Samanta, 2021; Klehm et al., 2014; Canadian Clobazam Cooperative Group, 1991)**	Used for Lennox-Gastaut syndrome, drug-resistant epilepsy, and adjunct for other seizures **(Gauthier & Mattson, 2015; Ng & Collins, 2007).**
Formulation	Oral suspension is preferred for accurate dosing **(Klehm et al., 2014).**	Tablets, film, or suspension **(Ng & Collins, 2007).**
Starting Dose	It is given weight based: 0.125–0.5 mg/kg twice daily **(Klehm et al., 2014).**	Typically, 5–10 mg/day, and can be up to 40mg/day based on the situation of the patient **(Ng & Collins, 2007).**
Dosing Flexibility	High—dose tailored by weight and age **(Klehm et al., 2014).**	Standardized dosing; it can be adjusted based on the patient's tolerability **(Ng & Collins, 2007).**
Efficacy	Well tolerated in most children;67–77% of people show significant seizure reduction **(Klehm et al., 2014).**	77% show seizure reduction in drug-resistant epilepsy **(Gauthier & Mattson).**
Side Effects	drowsiness, irritability, mood swings; rarely severe side effects **(Klehm et al., 2014).**	Somnolence, lethargy, mood changes; less sedation than other benzodiazepines **(Ng & Collins, 2007).**
Special Considerations	Oral suspension is essential for children <6 years **(Klehm et al., 2014).**	A lower starting dose may be needed in the elderly or poor metabolizers **(Ng & Collins, 2007).**
Monitoring	Growth, weight, behavioural changes, seizure frequency and many more tests in some interval of time **(Klehm et al., 2014).**	Mood, cognition, sedation, seizure control and many more tests in some interval of time **(Gauthier & Mattson).**
Compliance	Improved with liquid formulations and tailored dosing **(Klehm et al., 2014).**	Good, especially with flexible formulations **(Ng & Collins, 2007).**
Regulatory Approval	FDA-approved for children ≥2 years (LGS) **(Klehm et al., 2014).**	FDA-approved for adults with LGS and as an adjunct for other seizure types **(Gauthier & Mattson).**

Table: -6 -Clobazam usage in different age groups of people

9.2. Usage of carbamazepine in different age groups

Children		Adult
Indication	Mainly used for partial (focal), generalized Tonic-Clonic, and mixed seizure types **(Pellock, 1987; Crepeau et al., 2012).**	Used commonly in the case of partial, generalized Tonic-Clonic, and mixed seizures **(Kehoe & Haw, 2020; Motika & Smith, 2010).** It is also used for trigeminal neuralgia and bipolar disorder **(Kehoe & Haw, 2020).**
Formulation	Oral suspension, chewable tablets, or standard tablets **(Crepeau et al., 2012).**	Tablets, extended-release tablets/capsules, oral suspension **(Kehoe & Haw, 2020).**
Starting Dose	<6 years: 10–20 mg/kg/day in 2–3 doses. 6–12 years: 100 mg twice daily, adjusted as needed **(Crepeau et al., 2012).**	≥12 years: 200 mg twice daily, increased as needed. It can be extended up to 1000–1600 mg/day depending on the patient's situation **(Kehoe & Haw, 2020).**
Dosing Flexibility	Dose based on age and weight **(Crepeau et al., 2012).**	Standardized dosing **(Kehoe & Haw, 2020).**
Efficacy	Mostly effective for 80% of children with responsive seizure types **(Pellock, 1987).**	Very high efficacy for focal and generalized Tonic-Clonic seizures **(Kehoe & Haw, 2020).**
Side Effects	drowsiness, rash, GI (Gastrointestinal) upset **(Crepeau et al., 2012).**	Rash, dizziness, drowsiness, GI upset, hematologic toxicity, rare severe skin reactions **(Kehoe & Haw, 2020).**
Special Considerations	Higher clearance and shorter half-life in children **(Crepeau et al., 2012).**	Keep an eye out for possible drug interactions (like the CYP3A4 enzyme becoming more active), especially if you're taking several medications together **(Motika & Smith, 2010).**
Monitoring	Growth, weight, blood counts, liver function, and seizure control **(Crepeau et al., 2012).**	Blood counts, liver/kidney function, drug interactions, and seizure control **(Kehoe & Haw, 2020).**
Compliance	Liquid/chewable forms improve adherence **(Pellock, 1987).**	Extended-release medications help adults stick to their treatment plan **(Motika & Smith, 2010).**
Regulatory Approval	Approved for all ages; dosage set done by Neurologist **(Pellock, 1987).**	Approved for adults and children **(Kehoe & Haw, 2020).**

Table: -7 – Carbamazepine usage in different age groups of people

10. Use other than an anticonvulsant drug

10.1. Use of clobazam other than anticonvulsant drug

I. Anxiolytic (for anxiety) **(Brogden et al., 1980; Lafleur, 2016; DeVane, 2016)**

II. Adjunct in severe insomnia **(Smith, 2009; DeVane, 2016)**

III. Muscle relaxant **(Wikipedia, 2025; Toxin and Toxin Target Database, n.d.)**

IV. Adjunct in certain psychiatric disorders **(Robertson, 1986; Lafleur, 2016; Okuma & Kishimoto, 1998).**

10.2. Use of Carbamazepine other than an anticonvulsant drug

I. Mood stabilizer in bipolar **disorder (Okuma & Kishimoto, 1998; Kravitz & Fawcett, 1987).**

II. First-line treatment for this severe facial pain disorder **(Porter, 2008; Smith, 2009)**

III. In case of Glossopharyngeal neuralgia.

IV. Reduce alcohol withdrawal symptoms (**Barrons & Roberts, 2010; Schweizer et al., 1991; Ries et al., 1989**).

11. Conclusion

Clobazam, as well as Carbamazepine, are both very essential and effective medicines in the treatment of epilepsy as well as other neurological disorders **(Gauthier & Mattson, 2015; Wheless & Constantinou, 1997)**. They vary in side impacts, preferences, impediments, poisonous quality, etc., for diverse populations and are suited to the nature of the individual **(Kehoe & Haw, 2020; Bala & Vora, 2016).** Clobazam generally has fewer adverse biologic side effects and less potential for adverse event-related withdrawal, and is well-suited to many adults and children **(Bawden et al., 1999; Klehm et al., 2014; Gauthier & Mattson, 2015).** Then too, Carbamazepine is 1st choice in case of focal as well as partial epilepsy **(French, 1994; Marson et al., 2002).** But it causes severe side effects such as skin eruption, hematologic disorders, and several drug interactions **(Kehoe & Haw, 2020; Pellock, 1987; Matalon et al., 2002)**. Ultimately, preference of one over the other should be given, taking several things into mind, such as age, type of seizure, timing, tolerance capacity of one over the other, and life quality.Continued comparative studies and personalized medicine approaches are essential to optimize epilepsy treatment outcomes **(Samanta, 2021; French, 1994; Strzelczyk & Schubert-Bast, 2022).**

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