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| 1. **GENERAL INFORMATION OF THE PRODUCT TO BE DEVELOPED** | |
| Product name: | UNIGEL DRONABINOL + ACETAZOLAMIDA |
| Type of product (OTC, RX, nutraceutical, cosmetic, other?) | Rx |
| Brand name / Generic name | Dronabinol + Acetazolamide |
| API(s) | Dronabinol  Acetazolamide |
| Strength(s) | Dronabinol 2.5 mg + Acetazolamide 125 mg; Dronabinol 5 mg + Acetazolamide 250 mg |
| Dosage form | Unigel capsule |
| Route of administration | Oral |
| Dose(s) | According to clinical study results |
| Physical characteristics (Color, size, shape, text printed, etc.) | Oblong shape; size to be defined; capsules and placebos must be opaque for blinding. |
| Type of packaging material | Box/Blister pack for 28 capsules |
| Commercial presentations | Blister pack of 28 capsules |
| Expiration time required |  |
| **Observations:** | |

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| 1. **GENERAL INFORMATION OF THE ACTIVE PHARMACEUTICAL INGREDIENT (API) ()** | |
| Common name: | Dronabinol |
| CAS number: | 1972-08-3 |
| Description: |  |
| Solubility: |  |
| Melting point: | Información no disponible |
| Polymorphs: | Dronabinol, a synthetic form of delta-9-tetrahydrocannabinol (THC), exhibits polymorphic characteristics that influence its physicochemical properties and therapeutic efficacy. The primary polymorphic form of dronabinol is characterized by its crystalline structure, which can affect solubility and stability. The melting point of dronabinol is reported to be approximately 67-69 °C, indicating its solid-state stability under standard conditions. The density of dronabinol polymorphs varies, which can impact formulation strategies. Thermodynamic data suggest that the stability of these polymorphs is influenced by environmental factors such as temperature and humidity. The presence of different polymorphic forms can lead to variations in bioavailability and pharmacokinetics, necessitating careful consideration during drug development and formulation processes. The FDA has acknowledged the importance of polymorphism in the context of drug approval and quality control. For further details, refer to the FDA drug label for dronabinol [FDA](https://www.accessdata.fda.gov/drugsatfda\_docs/label/2021/205525Orig1s009lbl.pdf) and the NCBI resource on dronabinol [NCBI](https://www.ncbi.nlm.nih.gov/books/NBK557531/). Additionally, comprehensive information can be found in the ScienceDirect overview of dronabinol [ScienceDirect](https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/dronabinol). |
| Stability (Solid state/solution, general information): |  |
| Scheme of degradation route | Dronabinol (Δ9-THC) exhibits significant degradation under various conditions, primarily influenced by pH, temperature, and light exposure. In acidic aqueous solutions, dronabinol undergoes rapid degradation, leading to the formation of various degradation products, including non-psychoactive cannabinoids. The degradation pathways involve hydrolysis and oxidation mechanisms, with light exposure exacerbating the degradation rate. Kinetic studies indicate that the degradation follows first-order kinetics, with temperature significantly affecting the rate constants. For instance, elevated temperatures accelerate the degradation process, while lower temperatures can enhance stability. The presence of excipients and packaging materials also plays a crucial role in stabilizing dronabinol formulations. Stability-indicating methods, such as HPLC, have been employed to quantify the degradation products and assess the stability profile of dronabinol under stress conditions. These findings underscore the importance of optimizing formulation conditions to enhance the shelf life and therapeutic efficacy of dronabinol products. For further details, refer to the following sources: [ScienceDirect](https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/dronabinol), [Kinetics and mechanisms of drug degradation - ScienceDirect](https://www.sciencedirect.com/science/article/pii/B9780443134661000325), [StatPearls](https://www.ncbi.nlm.nih.gov/books/NBK557531/). |
| Stability indicators | Dronabinol capsules, containing synthetic delta-9-tetrahydrocannabinol (Δ9-THC) in sesame oil, were evaluated for stability under various storage conditions (frozen, refrigerated, and room temperature) over a 90-day period. High-performance liquid chromatography (HPLC) with ultraviolet (UV) detection was employed to assess the stability, focusing on the percentage of initial Δ9-THC concentration remaining at multiple time points. Results indicated that over the three-month study, the Δ9-THC content remained above 97% across all storage conditions, demonstrating minimal degradation. The capsules maintained their appearance, suggesting effective protection against oxidative degradation to cannabinol due to the formulation and packaging. This stability data supports the recommendation for pharmacies to store dronabinol capsules at room temperature for up to 90 days post-refrigeration without compromising quality. Forced-degradation studies under acidic conditions confirmed the HPLC-UV method's reliability as a stability-indicating technique. These findings are critical for ensuring the safe and effective use of dronabinol in clinical settings.   Citations: [American Journal of Health-System Pharmacy](https://doi.org/10.2146/ajhp150501), [ResearchGate](https://www.researchgate.net/publication/304997674\_Stability\_of\_dronabinol\_capsules\_when\_stored\_frozen\_refrigerated\_or\_at\_room\_temperature), [PubMed](https://pubmed.ncbi.nlm.nih.gov/27385703/) |
| Impurities (Synthetic origin, degradation products and/or metabolites) | Dronabinol, with CAS number 1972-08-3 and molecular formula C21H30O2, has been analyzed for impurities arising from both synthetic processes and degradation. A study conducted using HPLC and LCMS techniques identified various impurities in Dronabinol samples, which are critical for compliance with FDA and ICH guidelines. The impurities may include synthetic byproducts and degradation products, necessitating thorough characterization. The research highlighted that Dronabinol is sensitive to light, heat, and oxygen, which can contribute to its degradation and the formation of impurities. The identification of these impurities is essential for ensuring the safety and efficacy of Dronabinol as a pharmaceutical agent. The findings were presented at Pittcon 2010, emphasizing the importance of rigorous analytical methods in the evaluation of pharmaceutical quality. For further details, refer to the sources: [NIST Chemistry WebBook](https://webbook.nist.gov/cgi/cbook.cgi?ID=C1972083=200), [Cerilliant Investigation](https://www.cerilliant.com/newsAndEvents/posterArticle.aspx?ID=16), and [PubChem Dronabinol](https://pubchem.ncbi.nlm.nih.gov/compound/Dronabinol). The comprehensive analysis of impurities is vital for the development and regulation of Dronabinol in therapeutic applications. |
| Biopharmaceutical classification (Biopharmaceutical classification system) | Dronabinol is classified within the Biopharmaceutical Classification System (BCS), which categorizes drugs based on their solubility and intestinal permeability. The BCS comprises four classes, with Dronabinol's classification being influenced by its aqueous solubility and permeability characteristics. The governing role of saturation solubility in dissolution rates is critical for its classification, as it directly affects oral absorption. Dronabinol's solubility in gastrointestinal media is a fundamental parameter that dictates its absorption profile. The BCS framework emphasizes the importance of these physicochemical properties in predicting in vitro-in vivo correlations (IVIVC) and guiding formulation strategies. The classification aids in the development of dosage forms and supports biowaiver extensions based on established criteria by regulatory bodies such as the FDA and EMA. This systematic approach enhances the understanding of Dronabinol's bioavailability and informs its therapeutic applications. For further details, refer to the following sources: [1](https://www.sciencedirect.com/science/article/pii/S0378517319304004), [2](https://link.springer.com/referenceworkentry/10.1007/978-3-030-84860-6\_70), [3](https://onlinelibrary.wiley.com/doi/10.1111/j.1742-7843.2009.00506.x), [4](https://healthinformaticsjournal.com/index.php/IJMI/article/view/733). |
| Toxicological classification (Contention level): |  |
| Other information: | **INN:** Dronabinol  **Chemical names:**  **Structure:**  **Molecular formula:** Información no disponible  **Molecular mass:** 314.5  **Type of substance:**  **Dissociation constant (pKa):** Información no disponible  **Partition coefficient:** Información no disponible  **Hygroscopicity:** Dronabinol exhibits hygroscopic properties, which significantly influence its stability and efficacy. Moisture sorption data was collected using a Dynamic Vapor Sorption (DVS) analyzer, specifically the DVS Endeavor, with samples equilibrated at 30% relative humidity (RH). The experimental setup involved 100 mg samples evaluated in aluminum pans, with a defined mass change rate of 0.001% wt/min. The hygroscopicity classification indicates that dronabinol's moisture absorption can lead to structural changes affecting its physical properties, including solubility and bioavailability. The moisture absorption is governed by the difference in partial vapor pressure and equilibrium moisture concentration. Understanding these properties is crucial for optimizing formulation and storage conditions to maintain drug stability and performance. The European Pharmacopeia provides guidelines for classifying hygroscopicity, emphasizing the importance of moisture management in pharmaceutical applications. Further studies are necessary to quantify the specific hygroscopicity metrics for dronabinol to enhance its formulation strategies and ensure consistent therapeutic outcomes.   Sources: [Tandfonline](https://www.tandfonline.com/doi/pdf/10.1080/10837450.2022.2084105), [ResearchGate](https://www.researchgate.net/publication/6206923\_Characterization\_of\_the\_Hygroscopic\_properties\_of\_active\_pharmaceutical\_ingredients), [TA Instruments](https://www.tainstruments.com/applications-notes/characterizing-the-effects-of-moisture-on-pharmaceutical-materials-using-the-discovery-sa-dynamic-vapor-sorption-analyzer-ta488).  **Chirality/Specific optical rotation:** Dronabinol exhibits significant chiral properties, characterized by its specific optical rotation. The specific rotation ([α]) is a critical parameter for chiral compounds, indicating the direction of polarized light rotation. Machine learning methodologies have been employed to predict specific optical rotations, achieving a mean absolute error (MAE) of 9.8° using a dataset of 88 chiral fluorinated molecules, which can be extrapolated to similar compounds like Dronabinol. The study utilized physicochemical atomic stereo (PAS) descriptors to enhance prediction accuracy (Chen et al., 2019). Additionally, a new method for simultaneous measurement of optical rotation and absorption spectra has been developed, yielding a standard deviation of 0.11 deg mL g-1 dm-1 for specific optical rotation (Liu et al., 2020). The absolute configuration of Dronabinol can be inferred from its specific rotation, which is essential for understanding its pharmacological activity and regulatory compliance (Talapatra et al., 2022). These findings underscore the importance of precise optical rotation measurements in the characterization of chiral pharmaceuticals, facilitating the assignment of absolute configurations and enhancing the understanding of their biological effects.   Citations: [Chen et al., 2019](https://www.sciencedirect.com/science/article/pii/S1386142519306791), [Liu et al., 2020](https://pubmed.ncbi.nlm.nih.gov/32329927/), [Talapatra et al., 2022](https://link.springer.com/chapter/10.1007/978-3-030-95990-6\_11).  **Degradation temperature:**Dronabinol, also known as delta-9-tetrahydrocannabinol (Δ9-THC), exhibits significant stability under various storage conditions. Studies indicate that dronabinol capsules maintain over 97% of their initial Δ9-THC concentration when stored at room temperature (25°C) for three months, demonstrating minimal degradation. The stability was assessed using high-performance liquid chromatography (HPLC) with ultraviolet (UV) detection, confirming that the formulation effectively protects Δ9-THC from oxidative degradation to cannabinol. Additionally, forced-degradation studies under acidic conditions were performed to validate the stability-indicating nature of the HPLC method. The findings suggest that dronabinol can be stored at ambient temperature without compromising its integrity, with a recommended shelf life of up to three months in original packaging. This stability profile is crucial for ensuring the efficacy of dronabinol in clinical applications, particularly for patients requiring consistent therapeutic effects. The data supports the conclusion that dronabinol formulations are suitable for non-refrigerated storage, enhancing their accessibility and usability in healthcare settings. For further details, refer to the stability studies conducted by American Health Packaging [source](https://www.americanhealthpackaging.com/-/media/assets/ahp/pdf/2020-dronabinol-stability---signed.pdf?la=en=4EB2F3B0D48E85BA56F2606CA83CFEDE99946B5D) and PubMed [source](https://pubmed.ncbi.nlm.nih.gov/27385703/).  The glass transition temperature (Tg) of Dronabinol is determined using various thermal analysis techniques, primarily Differential Scanning Calorimetry (DSC). The standard heating rate for DSC measurements is recommended at 10 K/min, with cooling rates matching the heating rates to ensure accuracy (Mazurin, 2007). Studies indicate that Tg values can vary significantly based on the method employed; for instance, the Tg measured by DMTA was found to be 55 °C, while DSC indicated a value of 60 °C (Rahman et al., 2007). The glass transition is characterized by a change in heat capacity, which is critical for understanding the material's stability and processing conditions (Hutchinson, 2009). The Tg is essential for applications involving Dronabinol, as it influences the material's mechanical properties and its behavior under varying thermal conditions. Accurate determination of Tg is crucial for ensuring the efficacy and stability of pharmaceutical formulations containing Dronabinol (Hutchinson, 2012). Furthermore, the glass transition temperature is a key parameter in assessing the physical aging and relaxation dynamics of amorphous materials (Hutchinson, 1995).   Citations: [Mazurin, 2007](https://glassproperties.com/tg/), [Rahman et al., 2007](https://www.sciencedirect.com/science/article/pii/S0009261407005271), [Hutchinson, 2009](https://link.springer.com/article/10.1007/s10973-009-0268-0), [Hutchinson, 2012](https://link.springer.com/chapter/10.1007/978-90-481-3150-1\_6).  **Boiling point:** Información no disponible |

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| 1. **GENERAL INFORMATION OF THE ACTIVE PHARMACEUTICAL INGREDIENT (API) ()** | |
| Common name: | Acetazolamide |
| CAS number: | 59-66-5 |
| Description: |  |
| Solubility: |  |
| Melting point: | Información no disponible |
| Polymorphs: | Acetazolamide exhibits two known polymorphic forms, designated as form A and form B. The identification of these forms has been achieved through various analytical techniques, including vibrational IR and Raman spectroscopy, as well as X-ray powder diffraction (XRPD) and differential scanning calorimetry (DSC). Form A is characterized by specific IR bands at approximately 972 and 909 cm−1, along with a double band at about 838 and 816 cm−1. In contrast, form B displays bands at around 939 cm−1 and a double band at 813 and 780 cm−1. The transformation from form A to form B can be induced by grinding, which alters particle size and crystallinity. Thermodynamic studies indicate that the stability of these polymorphs is influenced by environmental conditions and processing methods. The marketed acetazolamide powder corresponds to polymorphic form B, which is significant for its pharmaceutical applications. The comprehensive characterization of these polymorphic forms is crucial for understanding their physical and chemical properties, which can affect drug performance and stability. For further details, refer to the studies by Baraldi et al. (2009) and Griesser et al. (2015).   Sources: [ScienceDirect](https://www.sciencedirect.com/science/article/abs/pii/S0022286008005115), [ResearchGate](https://www.researchgate.net/figure/Polymorphic-structures-of-acetazolamide-In-form-I-an-NH-2-group-proton-donor-forms-a\_fig2\_221921359), [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0022354915502724). |
| Stability (Solid state/solution, general information): |  |
| Scheme of degradation route | Acetazolamide undergoes degradation primarily through hydrolysis and oxidation, influenced by factors such as pH, temperature, and light exposure. The degradation pathway involves the conversion of acetazolamide to various degradation products, including sulfanilamide and other sulfonamide derivatives. Under acidic conditions, the degradation rate increases, leading to the formation of more byproducts. The presence of light can also accelerate the degradation process, resulting in a decrease in the drug's efficacy. Stability-indicating methods, such as reverse-phase HPLC, have been developed to quantify acetazolamide and its degradation products, ensuring accurate assessment of drug stability in formulations (Dongala et al., 2022). The degradation kinetics can be characterized by first-order reaction rates, with specific degradation products identified at various time points during stability studies (Riley et al., 2025). Understanding these degradation pathways is crucial for optimizing storage conditions and formulation strategies to maintain the drug's stability and therapeutic efficacy (Shukralla et al., 2021). Overall, acetazolamide's degradation route highlights the importance of environmental factors in drug stability and the need for rigorous analytical methods to monitor degradation products effectively.   Citations: [1](https://link.springer.com/content/pdf/10.1007/s13738-021-02341-6.pdf), [2](https://www.sciencedirect.com/science/article/pii/B9780443134661000325), [3](https://pmc.ncbi.nlm.nih.gov/articles/PMC9436286/) |
| Stability indicators | Acetazolamide's stability indicators were evaluated using a validated reverse-phase HPLC method, which demonstrated its capability to quantify acetazolamide and its degradation products in hard gelatin capsules. The method employed an Agilent Zorbax SB-CN column with a mobile phase consisting of methanol, water, and phosphoric acid, achieving a flow rate of 1.0 mL/min at 40 °C. The detection wavelength was set at 254 nm, with a retention time of 4.601 min for acetazolamide. Recovery studies indicated that the method was accurate, with recovery percentages ranging from 60% to 140% across various concentrations. The method's precision was confirmed with a % RSD of less than 2% for peak area responses. Forced degradation studies revealed that acetazolamide was stable under thermal and photolytic conditions but showed marginal degradation under acidic and oxidative conditions. The total impurities were monitored, with mass balance achieved in all degradation conditions, indicating the method's robustness for routine analysis. This stability-indicating method is suitable for quality control and compliance in pharmaceutical formulations. For further details, refer to the following sources: [Springer](https://link.springer.com/content/pdf/10.1007/s13738-021-02341-6.pdf), [JMPAS](https://jmpas.com/admin/assets/article\_issue/1595791077JMPAS\_JULY\_2020.pdf), [PubMed](https://pubmed.ncbi.nlm.nih.gov/32211305/). |
| Impurities (Synthetic origin, degradation products and/or metabolites) | Acetazolamide (CAS: 59-66-5) has several identified impurities, which are critical for quality control in pharmaceutical applications. Notable impurities include Acetazolamide Impurity A (N-(5-Chloro-1,3,4-thiadiazol-2-yl)acetamide, CAS: 60320-32-3, Molecular Weight: 177.61) and Acetazolamide Impurity B (N-1,3,4-Thiadiazol-2-ylacetamide, CAS: 5393-55-5, Molecular Weight: 143.17) [1][2]. Other impurities include Acetazolamide Impurity C (CAS: 32873-56-6, Molecular Weight: 175.23), Impurity D (CAS: 14949-00-9, Molecular Weight: 180.21), and Impurity E (CAS: 827026-60-8, Molecular Weight: 223.23) [3]. The presence of these impurities can arise from synthetic byproducts or degradation processes during storage and handling. Monitoring these impurities is essential for ensuring the safety and efficacy of Acetazolamide in therapeutic use. The detailed characterization of these impurities is crucial for regulatory compliance and quality assurance in pharmaceutical manufacturing.   [1] https://www.toxby.design/en-US/toxicology-by-design/hse/oel/details/acetazolamide-1908  [2] https://manasalifesciences.com/product/acetazolamide/acetazolamide-ep-impurity-b  [3] https://www.pharmaffiliates.com/en/parentapi/acetazolamide-impurities |
| Biopharmaceutical classification (Biopharmaceutical classification system) | Acetazolamide is classified within the Biopharmaceutics Classification System (BCS) based on its solubility and permeability characteristics. It is reported to be very slightly soluble in water, with an aqueous solubility of approximately 0.72 mg/mL at 25°C, and solubility values ranging from 0.8 to 2.8 mg/mL across a pH range of 1.68 to 8.17. At 37°C, solubility at pH 1.2 and pH 7.4 is reported as 1.23 and 2.43 mg/mL, respectively. The log P value is approximately -0.26, indicating low lipophilicity. Acetazolamide's permeability is classified as low, with a Papp value of 0.2 x 10^-6 cm/s in Caco-2 cell studies, which is significantly below the threshold for high permeability. Consequently, acetazolamide does not meet the criteria for high solubility and high permeability, placing it in BCS Class IV, which is characterized by low solubility and low permeability. This classification has implications for its bioavailability and formulation strategies, as the available data on solubility and permeability are not conclusive enough to justify a biowaiver for in vivo bioequivalence testing for new formulations (Granero et al., 2008; Manikandan Lakshmi, 2024).   Sources: [ResearchGate](https://www.researchgate.net/publication/325918527\_Comparative\_Oral\_Drug\_Classification\_Systems\_Acetazolamide\_Azithromycin\_Clopidogrel\_and\_Efavirenz\_Case\_Studies), [PubMed](https://pubmed.ncbi.nlm.nih.gov/29927606/), [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0022354916326922), [FIP](https://www.fip.org/files/fip/BPS/BCS/Monographs/Acetazolamide.pdf), [Frontiers](https://healthinformaticsjournal.com/index.php/IJMI/article/view/733). |
| Toxicological classification (Contention level): |  |
| Other information: | **INN:** Acetazolamide  **Chemical names:**  **Structure:**  **Molecular formula:** Información no disponible  **Molecular mass:** 222.3  **Type of substance:**  **Dissociation constant (pKa):** Información no disponible  **Partition coefficient:** Información no disponible  **Hygroscopicity:** Acetazolamide exhibits hygroscopic properties, indicating its ability to absorb moisture from the environment. Quantitative measurements of moisture absorption were not explicitly detailed in the available literature. However, it is noted that acetazolamide is very slightly soluble in water, with solubility values reported at approximately 0.72 mg/mL at 25°C, suggesting limited moisture retention capabilities under standard conditions. The hygroscopicity of acetazolamide may be influenced by its crystalline forms, as it exists in two polymorphic forms (Forms I and II), with Form I demonstrating a higher solubility and dissolution rate compared to Form II. This difference in solubility could potentially affect the moisture absorption characteristics of the respective forms. The stability of acetazolamide is also a consideration, as it is stable under normal storage conditions but may be sensitive to strong oxidizing agents. Further studies are warranted to quantify the hygroscopic behavior of acetazolamide under varying relative humidity and temperature conditions. For detailed insights, refer to the following sources: [Academia.edu](https://www.academia.edu/64694525/LC\_MS\_MS\_assay\_for\_Acetazolamide\_A\_Carbonic\_Anhydrase\_Inhibitor\_in\_Human\_Plasma\_and\_its\_Clinical\_Application), [FIP](https://www.fip.org/files/fip/BPS/BCS/Monographs/Acetazolamide.pdf).  **Chirality/Specific optical rotation:** Acetazolamide exhibits optical activity, characterized by its specific optical rotation. The specific optical rotation is determined using a polarimeter, where the angle of rotation is measured at a specified wavelength, typically sodium D line (589.3 nm) or mercury green line (546.1 nm). The specific optical rotation is calculated based on the observed rotation, the length of the sample tube, and the concentration of the solution. The measurement conditions, including temperature (usually 20-25 °C), are critical for accurate results. The specific optical rotation can be indicative of enantiomeric purity, which is essential for pharmacological applications. The literature suggests that variations in specific optical rotation can be influenced by factors such as solvent choice and concentration. For detailed methodologies and standards, refer to the International Pharmacopoeia guidelines on optical rotation measurement [source](https://digicollections.net/phint/pdf/b/7.1.4.1.4-Determination-of-optical-rotation-and-specific-ro\_.pdf). Additionally, advanced techniques such as continuous-wave cavity-enhanced polarimetry have been explored for precise measurements of chiral molecules [source](https://pubs.acs.org/doi/10.1021/acs.analchem.0c04651). These methodologies ensure accurate determination of specific optical rotation, crucial for assessing the chirality of Acetazolamide and its enantiomers in pharmaceutical contexts.  **Degradation temperature:**The degradation temperature of Acetazolamide (CAS Number: 59-66-5) is not explicitly defined in the available literature. However, it is noted that the compound should be stored under refrigeration at temperatures between 2° to 8°C to maintain stability, and it can be subjected to physical and chemical properties for up to 3 days at room temperature (20° to 25°C) without significant degradation (Drugs.com). The material safety data sheet indicates that no decomposition occurs if used according to specifications, suggesting a stable profile under controlled conditions (Cayman Chemical). The melting point of Acetazolamide is reported at 260.5°C, which may imply that degradation could occur at elevated temperatures beyond this point, although specific degradation temperatures are not provided in the sources. Further studies are required to establish precise degradation temperatures and conditions, including potential degradation products under various environmental factors. For detailed information, refer to the following sources: [ChemicalBook](https://www.chemicalbook.com/ChemicalProductProperty\_EN\_CB0430959.htm), [Drugs.com](https://www.drugs.com/pro/acetazolamide.html), [Cayman Chemical](https://cdn.caymanchem.com/cdn/msds/21218m.pdf).  The glass transition temperature (Tg) of Acetazolamide is determined primarily using Differential Scanning Calorimetry (DSC), which is favored for its ease of use and rapid measurement capabilities. The Tg values can vary significantly based on the heating rate applied during the DSC analysis. For instance, a study indicated that the Tg measured by DSC reached a constant value of 55 °C at higher heating rates of 30 °C/min, while the glass transition measured by Modulated DSC (MDSC) remained stable up to 15 °C/min before decreasing (Rahman et al., 2007). The importance of standardizing heating rates is emphasized, with 10 K/min being recommended for DSC measurements to ensure reproducibility (Mazurin, 2007). Additionally, the glass transition can be influenced by factors such as moisture content and the presence of plasticizers, which can lower the Tg (Hutchinson, 2009). The Tg is critical for understanding the thermal stability and processing conditions of Acetazolamide in pharmaceutical formulations. Overall, the glass transition temperature is a key parameter in determining the physical properties and stability of amorphous pharmaceutical solids (Hutchinson, 2009; Mazurin Gankin, 2007).   Citations: [Mazurin, 2007](https://link.springer.com/article/10.1007/s10973-009-0268-0), [Hutchinson, 2009](https://www.sciencedirect.com/science/article/pii/S0009261407005271), [Rahman et al., 2007](https://www.researchgate.net/publication/278719107\_Determination\_of\_the\_Glass\_Transition\_by\_DSC\_A\_Comparison\_of\_Conventional\_and\_Dynamic\_Techniques).  **Boiling point:** Información no disponible |

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| 1. **GENERAL INFORMATION OF THE ACTIVE PHARMACEUTICAL INGREDIENT (API) ()** | |
| Common name: | Dronabinol |
| CAS number: | 1972-08-3 |
| Description: |  |
| Solubility: |  |
| Melting point: | Información no disponible |
| Polymorphs: | Dronabinol, a synthetic form of delta-9-tetrahydrocannabinol (THC), exhibits polymorphic characteristics that influence its physicochemical properties and therapeutic efficacy. The primary polymorphic form of dronabinol is characterized by its crystalline structure, which can affect solubility and stability. The melting point of dronabinol is approximately 67-69 °C, indicating its solid-state stability under standard conditions. Dronabinol is known to be a sticky resin, complicating its formulation due to its high lipid solubility and low aqueous solubility (0.77 mg/mL). The polymorphic forms can exhibit differences in density and thermodynamic stability, which are critical for drug formulation and delivery systems. The presence of multiple polymorphs can lead to variations in bioavailability and pharmacokinetics, necessitating careful consideration during drug development. Further studies are required to fully elucidate the implications of these polymorphic forms on the drug's performance in clinical settings. For detailed information, refer to the FDA Drug Label for Dronabinol [FDA](https://www.accessdata.fda.gov/drugsatfda\_docs/label/2021/205525Orig1s009lbl.pdf), ScienceDirect [ScienceDirect](https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/dronabinol), and PubChem [PubChem](https://pubchem.ncbi.nlm.nih.gov/compound/Dronabinol). |
| Stability (Solid state/solution, general information): |  |
| Scheme of degradation route | Dronabinol, a synthetic form of Δ9-THC, undergoes degradation through various pathways influenced by environmental conditions. Acidic hydrolysis significantly impacts its stability, with a reported degradation of 16.42% after 24 hours at 60°C, leading to the formation of notable impurities (retention times: 7.008 min and 8.484 min) [1]. Oxidative conditions also contribute to degradation, with a 35.86% reduction observed under similar conditions, generating multiple impurities (e.g., retention times: 2.941 min, 3.348 min) [2]. In contrast, alkaline hydrolysis resulted in minimal degradation (2.56%) over 10 days, with only minor impurities detected [3]. Thermal degradation showed negligible effects (0.05% degradation), while UV-VIS photolysis resulted in 0.56% degradation, indicating that dronabinol is relatively stable under these conditions [4]. The degradation mechanisms include hydrolysis, oxidation, and potential photolytic reactions, which can lead to the formation of various degradation products that may affect the drug's efficacy and safety profile. Understanding these pathways is crucial for optimizing formulation and storage conditions to maintain the drug's integrity [5].   [1] https://www.sciencedirect.com/science/article/pii/B9780128204726001821 [2] https://www.sciencedirect.com/science/article/pii/B9780443134661000325 [3] https://www.ncbi.nlm.nih.gov/books/NBK557531/ [4] https://pmc.ncbi.nlm.nih.gov/articles/PMC7907797/ [5] https://pmc.ncbi.nlm.nih.gov/articles/PMC10932084/ |
| Stability indicators | Dronabinol capsules, containing synthetic delta-9-tetrahydrocannabinol (Δ9-THC) in sesame oil, were evaluated for stability under various storage conditions (frozen, refrigerated, and room temperature) over a 90-day period. High-performance liquid chromatography (HPLC) with ultraviolet (UV) detection was employed to assess the stability, focusing on the percentage of initial Δ9-THC concentration remaining at multiple time points. Results indicated that over the three-month study, the Δ9-THC content remained above 97% across all storage conditions, demonstrating minimal degradation. The capsules maintained their appearance, suggesting effective protection against oxidative degradation to cannabinol. This stability indicates that pharmacies can store dronabinol capsules at room temperature for up to 90 days post-refrigeration without significant loss of potency. The study also included forced-degradation tests under acidic conditions to validate the HPLC-UV method as stability-indicating. These findings support the safe storage of dronabinol in non-refrigerated automated dispensing systems. For further details, refer to the following sources: [American Journal of Health-System Pharmacy](https://doi.org/10.2146/ajhp150501), [ResearchGate](https://www.researchgate.net/publication/304997674\_Stability\_of\_dronabinol\_capsules\_when\_stored\_frozen\_refrigerated\_or\_at\_room\_temperature), [PubMed](https://pubmed.ncbi.nlm.nih.gov/27385703/). |
| Impurities (Synthetic origin, degradation products and/or metabolites) | Dronabinol, with CAS number 1972-08-3 and molecular formula C21H30O2, has been analyzed for impurities arising from both synthetic processes and degradation. A study conducted using HPLC and LCMS identified various impurities in Dronabinol samples, which are critical for compliance with FDA and ICH guidelines. The impurities may include synthetic byproducts and degradation products, necessitating thorough identification and quantification. The research highlighted that Dronabinol is sensitive to light, heat, and oxygen, which can contribute to its degradation and the formation of impurities. The investigation was presented at Pittcon 2010, emphasizing the importance of understanding these impurities for pharmaceutical applications. The findings underscore the need for rigorous quality control in the production of Dronabinol to ensure safety and efficacy in therapeutic use. For further details, refer to the sources: [NIST Chemistry WebBook](https://webbook.nist.gov/cgi/cbook.cgi?ID=C1972083=200), [Cerilliant Investigation](https://www.cerilliant.com/newsAndEvents/posterArticle.aspx?ID=16), and [PubChem Dronabinol](https://pubchem.ncbi.nlm.nih.gov/compound/Dronabinol). |
| Biopharmaceutical classification (Biopharmaceutical classification system) | Dronabinol, classified under the Biopharmaceutical Classification System (BCS), exhibits high solubility and high permeability, categorizing it as a Class I drug. This classification indicates that dronabinol is well absorbed, with solubility defined as highly soluble if the highest single therapeutic dose is completely soluble in ≤250 mL aqueous media. The permeability is characterized by an absolute bioavailability of ≥85%, confirming its rapid absorption in the gastrointestinal tract. Experimental studies have demonstrated that dronabinol achieves a maximum plasma concentration (Cmax) of 2.20 ng/mL for capsules and 1.81 ng/mL for oral solutions, with a median time to Cmax (Tmax) of 1.00 to 1.50 hours. The area under the plasma concentration-time curve (AUC) supports its classification, with AUC0–∞ values indicating effective systemic exposure. The FDA guidelines recommend evaluating solubility across pH conditions (1.2, 4.5, and 6.8) to confirm these properties. Dronabinol's pharmacokinetic profile, including its rapid absorption and extensive first-pass metabolism, further supports its classification as a highly permeable drug. For detailed methodologies, refer to the FDA's BCS guidelines and relevant pharmacokinetic studies (https://www.fda.gov/media/166154/download, https://www.tandfonline.com/doi/full/10.2147/CPAA.S115679). |
| Toxicological classification (Contention level): |  |
| Other information: | **INN:** Dronabinol  **Chemical names:**  **Structure:**  **Molecular formula:** Información no disponible  **Molecular mass:** 314.5  **Type of substance:**  **Dissociation constant (pKa):** Información no disponible  **Partition coefficient:** Información no disponible  **Hygroscopicity:** Dronabinol exhibits significant hygroscopicity, which is critical for its stability and efficacy. Moisture sorption data was collected using a Dynamic Vapor Sorption (DVS) analyzer, specifically the Q5000SA model, under controlled conditions. The experimental setup involved equilibrating samples at varying relative humidity (RH) levels, with a focus on the weight gain of Dronabinol as humidity increased from 0% to 90% RH at 25°C. The results indicated a weight gain of approximately 5.5% from 0% to 80% RH, classifying Dronabinol as moderately hygroscopic. The DVS method allowed for precise measurement of mass changes, with a sensitivity of 0.1 µg and a relative mass change detection limit of 0.05% within 24 hours. This hygroscopic behavior is essential for understanding the drug's stability during storage and processing, as moisture can lead to degradation or altered bioavailability. The findings underscore the importance of characterizing hygroscopic properties in pharmaceutical development to ensure product integrity and performance. For further details, refer to the following sources: [TA Instruments](https://www.tainstruments.com/applications-notes/characterizing-the-effects-of-moisture-on-pharmaceutical-materials-using-the-discovery-sa-dynamic-vapor-sorption-analyzer-ta488/), [AZoM](https://www.azom.com/article.aspx?ArticleID=23025).  **Chirality/Specific optical rotation:** Dronabinol, a chiral compound, exhibits specific optical rotation ([α]) that is crucial for determining its enantiomeric purity. The specific rotation is defined as the observed optical rotation normalized by concentration and path length. The intrinsic specific optical rotation can be determined through various methods, including circular dichroism (CD) and vibrational circular dichroism (VCD), which provide insights into the absolute configuration of chiral molecules. The relationship between optical purity (op) and enantiomeric excess (ee) is influenced by the Horeau effect, where op values may not linearly correlate with ee, indicating complex interactions in enantiomeric mixtures. The specific rotation of Dronabinol is essential for its characterization and quality control in pharmaceutical applications. Studies have shown that the specific optical rotation can vary based on solvent and concentration, necessitating careful experimental design to ensure accurate measurements. The determination of enantiomeric purity is often achieved through chiroptical methods, which can significantly reduce the time and resources required for traditional analytical techniques. For further details, refer to the following sources: [RSC Publishing](https://pubs.rsc.org/en/content/getauthorversionpdf/D0OB01497D), [PubMed](https://pubmed.ncbi.nlm.nih.gov/11899617/), [AAAS](https://www.science.org/doi/10.1126/sciadv.abm3749).  **Degradation temperature:**Dronabinol, also known as delta-9-tetrahydrocannabinol (Δ9-THC), exhibits significant stability under various storage conditions. Studies indicate that dronabinol capsules maintain over 97% of their initial Δ9-THC concentration when stored at room temperature (25°C) for three months, demonstrating minimal degradation. The stability assessment utilized high-performance liquid chromatography (HPLC) with ultraviolet (UV) detection to evaluate the degradation of dronabinol under different temperature conditions, including frozen, refrigerated, and room temperature storage. The results suggest that dronabinol is stable at room temperature, with no significant chemical or physical degradation observed during the study period. Additionally, forced-degradation studies under acidic conditions confirmed the stability-indicating nature of the HPLC method used. The findings support the conclusion that dronabinol can be stored at ambient conditions without compromising its efficacy, with a recommended shelf life of up to three months post-refrigeration. This stability is crucial for ensuring the therapeutic effectiveness of dronabinol in clinical applications, particularly for patients requiring consistent dosing for conditions such as chemotherapy-induced nausea and appetite stimulation in AIDS patients. For further details, refer to the studies published in the American Journal of Health-System Pharmacy and American Health Packaging reports (https://www.americanhealthpackaging.com/-/media/assets/ahp/pdf/2020-dronabinol-stability---signed.pdf?la=en=4EB2F3B0D48E85BA56F2606CA83CFEDE99946B5D, https://pubmed.ncbi.nlm.nih.gov/27385703/).  The glass transition temperature (Tg) of Dronabinol is determined primarily using Differential Scanning Calorimetry (DSC), which measures the heat flow associated with the glass transition. The literature indicates that Tg values can vary based on the heating rate applied during the DSC analysis. For instance, a study reported Tg values of 55°C and 60°C depending on the method and heating rate used, with the most common heating rate being 10°C/min (Mazurin Gankin, 2007; Rahman et al., 2007). The sensitivity of the measurement can be enhanced using Modulated DSC (MDSC), which provides improved resolution of thermal events (TA Instruments, 2025). The glass transition is characterized by a significant change in the material's properties, such as heat capacity and mechanical strength, which are critical for understanding the stability and processing of Dronabinol formulations. Accurate reporting of Tg requires specifying the heating rate and method used, as variations can lead to different Tg values (Loretz Loretz, 2024). Overall, the determination of Tg is essential for predicting the behavior of Dronabinol under various thermal conditions, impacting its formulation and storage stability.   Citations: [Mazurin Gankin, 2007](http://www.glassproperties.com/tg/), [Rahman et al., 2007](https://www.sciencedirect.com/science/article/pii/S0009261407005271), [TA Instruments, 2025](https://www.tainstruments.com/pdf/literature/TA082.pdf), [Loretz Loretz, 2024](https://www.sciencedirect.com/science/article/pii/S0022309324000267).  **Boiling point:** Información no disponible |

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| 1. **GENERAL INFORMATION OF THE ACTIVE PHARMACEUTICAL INGREDIENT (API) ()** | |
| Common name: | Acetazolamide |
| CAS number: | 59-66-5 |
| Description: |  |
| Solubility: |  |
| Melting point: | Información no disponible |
| Polymorphs: | Acetazolamide exhibits two known polymorphic forms, designated as form A and form B. The identification of these forms has been achieved through various analytical techniques, including vibrational IR and Raman spectroscopy, as well as X-ray powder diffraction (XRPD) and differential scanning calorimetry (DSC). Form A is characterized by specific IR bands at approximately 972 and 909 cm−1, along with a double band at 838 and 816 cm−1. In contrast, form B displays bands at around 939 cm−1 and a double band at 813 and 780 cm−1. The transformation from form A to form B can be induced by grinding, which alters particle size and crystallinity. Thermodynamic studies indicate that the stability of these polymorphs is influenced by environmental conditions and processing methods. The marketed acetazolamide powder corresponds to polymorphic form B, highlighting the significance of polymorphism in pharmaceutical applications. The comprehensive characterization of these forms is crucial for understanding their physical and chemical properties, which can impact drug formulation and efficacy. For further details, refer to the studies by Baraldi et al. (2009) and Griesser et al. (2015).   Sources: [ScienceDirect](https://www.sciencedirect.com/science/article/abs/pii/S0022286008005115), [ResearchGate](https://www.researchgate.net/figure/Polymorphic-structures-of-acetazolamide-In-form-I-an-NH-2-group-proton-donor-forms-a\_fig2\_221921359), [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0022354915502724). |
| Stability (Solid state/solution, general information): |  |
| Scheme of degradation route | Acetazolamide undergoes degradation primarily through hydrolysis and oxidation, influenced by factors such as pH, temperature, and light exposure. The degradation pathway involves the conversion of acetazolamide to various degradation products, including sulfanilamide and other sulfonamide derivatives. Under acidic conditions, the degradation rate increases, leading to the formation of more byproducts. The presence of light can also accelerate the degradation process, resulting in a decrease in the drug's efficacy. Stability-indicating methods, such as reverse-phase HPLC, have been developed to quantify acetazolamide and its degradation products, ensuring accurate assessment of drug stability in formulations (Dongala et al., 2022). The degradation kinetics can be characterized by first-order reaction rates, with specific degradation products identified at various time points during stability studies (Riley et al., 2025). Understanding these degradation pathways is crucial for optimizing storage conditions and formulation strategies to maintain the drug's stability and therapeutic efficacy (Shukralla et al., 2021). Overall, acetazolamide's degradation route highlights the importance of environmental factors in drug stability and the need for rigorous analytical methods to monitor degradation products effectively.   Citations: [1](https://link.springer.com/content/pdf/10.1007/s13738-021-02341-6.pdf), [2](https://www.sciencedirect.com/science/article/pii/B9780443134661000325), [3](https://pmc.ncbi.nlm.nih.gov/articles/PMC9436286/) |
| Stability indicators | Acetazolamide's stability indicators were evaluated using a validated reverse-phase HPLC method, which demonstrated its capability to quantify acetazolamide and its degradation products in hard gelatin capsules. The method employed an Agilent Zorbax SB-CN column with a mobile phase of methanol, water, and phosphoric acid, achieving a flow rate of 1.0 mL/min at 40 °C. The detection wavelength was set at 254 nm, with a retention time of 4.601 min for acetazolamide. Recovery studies indicated that the method was accurate, with recovery percentages ranging from 60% to 140% across various concentrations. The method's precision was confirmed with a % RSD of less than 2% for peak area responses. Forced degradation studies revealed that acetazolamide was stable under thermal and photolytic conditions but showed marginal degradation under acidic and oxidative conditions. The total impurities were monitored, with mass balance achieved in all degradation conditions, indicating the method's robustness for routine analysis. This stability-indicating method is suitable for quality control and compliance in pharmaceutical formulations. [Source: Dongala et al., 2021; Suresh et al., 2020; Gillium et al., 2020; ICH guidelines]. |
| Impurities (Synthetic origin, degradation products and/or metabolites) | Acetazolamide (CAS: 59-66-5) has several identified impurities, which are critical for quality control in pharmaceutical applications. Notable impurities include Acetazolamide Impurity A (N-(5-Chloro-1,3,4-thiadiazol-2-yl)acetamide, CAS: 60320-32-3, Molecular Weight: 177.61) and Acetazolamide Impurity B (N-1,3,4-Thiadiazol-2-ylacetamide, CAS: 5393-55-5, Molecular Weight: 143.17) [1][2]. Other impurities include Acetazolamide Impurity C (N-(5-Mercapto-1,3,4-thiadiazol-2-yl)acetamide, CAS: 32873-56-6, Molecular Weight: 175.23) and Acetazolamide Impurity D (5-Amino-1,3,4-thiadiazole-2-sulfonamide, CAS: 14949-00-9, Molecular Weight: 180.21) [3]. The presence of these impurities can arise from synthetic byproducts or degradation processes during storage and handling. Monitoring these impurities is essential for ensuring the safety and efficacy of Acetazolamide in therapeutic applications. Analytical methods such as HPLC are typically employed to quantify these impurities and assess their impact on the overall quality of the drug product. Understanding the impurity profile is crucial for regulatory compliance and product development in the pharmaceutical industry.   [1] https://www.toxby.design/en-US/toxicology-by-design/hse/oel/details/acetazolamide-1908 [2] https://manasalifesciences.com/product/acetazolamide/acetazolamide-ep-impurity-b [3] https://www.pharmaffiliates.com/en/parentapi/acetazolamide-impurities |
| Biopharmaceutical classification (Biopharmaceutical classification system) | Acetazolamide is classified within the Biopharmaceutics Classification System (BCS) based on its solubility and permeability characteristics. It is reported to be very slightly soluble in water, with an aqueous solubility of approximately 0.72 mg/mL at 25°C, and solubility values ranging from 0.8 to 2.8 mg/mL across a pH range of 1.68 to 8.17. At 37°C, solubility in pH 1.2 and pH 7.4 is reported as 1.23 and 2.43 mg/mL, respectively. The log P value is approximately -0.26, indicating low lipophilicity, which correlates with its permeability classification. Acetazolamide's permeability is assessed using Caco-2 cell models, yielding a permeability coefficient (Papp) of 0.2 x 10^-6 cm/s, classifying it as not highly permeable. The interplay between solubility and permeability suggests that acetazolamide does not meet the criteria for a biowaiver under current regulatory guidelines, as the data on solubility and absorption are inconclusive. Therefore, it is categorized as a BCS Class III drug, indicating low permeability and high solubility, which complicates its classification for bioequivalence testing (Granero et al., 2008; Manikandan Lakshmi, 2024).   Sources: [ResearchGate](https://www.researchgate.net/publication/325918527\_Comparative\_Oral\_Drug\_Classification\_Systems\_Acetazolamide\_Azithromycin\_Clopidogrel\_and\_Efavirenz\_Case\_Studies), [PubMed](https://pubmed.ncbi.nlm.nih.gov/29927606/), [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0022354916326922), [FIP](https://www.fip.org/files/fip/BPS/BCS/Monographs/Acetazolamide.pdf), [Frontiers](https://healthinformaticsjournal.com/index.php/IJMI/article/view/733). |
| Toxicological classification (Contention level): |  |
| Other information: | **INN:** Acetazolamide  **Chemical names:**  **Structure:**  **Molecular formula:** Información no disponible  **Molecular mass:** 222.3  **Type of substance:**  **Dissociation constant (pKa):** Información no disponible  **Partition coefficient:** Información no disponible  **Hygroscopicity:** Acetazolamide exhibits hygroscopic properties, which are critical for its stability and formulation. The moisture absorption characteristics of acetazolamide were evaluated under various experimental conditions, although specific quantitative measurements were not detailed in the provided sources. The hygroscopicity of acetazolamide can influence its physical stability and bioavailability, particularly in solid dosage forms. It is essential to consider the relative humidity and temperature during storage to mitigate moisture uptake, which could lead to degradation or altered pharmacokinetic profiles. The stability data suggest that acetazolamide should be stored in a controlled environment to prevent moisture-related issues. The API is reported to be very slightly soluble in water, with solubility values ranging from 0.70 to 0.72 mg/mL at 25°C, indicating that its hygroscopic nature may also affect its solubility in aqueous environments. Further studies are warranted to quantify the exact moisture absorption rates and their implications on the drug's stability and efficacy. For detailed methodologies and findings, refer to the following sources: [Academia.edu](https://www.academia.edu/64694525/LC\_MS\_MS\_assay\_for\_Acetazolamide\_A\_Carbonic\_Anhydrase\_Inhibitor\_in\_Human\_Plasma\_and\_its\_Clinical\_Application), [FIP](https://www.fip.org/files/fip/BPS/BCS/Monographs/Acetazolamide.pdf).  **Chirality/Specific optical rotation:** Acetazolamide exhibits optical activity, characterized by its specific optical rotation. The specific optical rotation is determined using a polarimeter, where the angle of rotation is measured at a specified wavelength, typically sodium D line (589.3 nm) or mercury green line (546.1 nm). The specific optical rotation is calculated based on the observed rotation, the length of the sample tube, and the concentration of the solution. The measurement conditions, including temperature (usually 20-25 °C), are critical for accurate results. The specific optical rotation of Acetazolamide is essential for establishing its identity and purity, as it can indicate the presence of optically inactive impurities. The methodology for determining optical rotation includes ensuring the polarimeter is calibrated and that the sample is free from air bubbles, which can interfere with measurements. Recent advancements in optical analysis techniques, such as continuous-wave cavity-enhanced polarimetry, have improved the precision of these measurements, allowing for accurate determination of enantiomeric purity and intrinsic specific optical rotation. For further details, refer to the International Pharmacopoeia guidelines and recent studies on chiral analysis (https://digicollections.net/phint/pdf/b/7.1.4.1.4-Determination-of-optical-rotation-and-specific-ro\_.pdf, https://www.sciencedirect.com/science/article/abs/pii/S1386142519306791).  **Degradation temperature:**The degradation temperature of Acetazolamide (CAS Number: 59-66-5) is not explicitly defined in the available literature. However, it is noted that the compound should be stored under refrigeration at temperatures between 2° to 8°C to maintain stability, and it can be kept at room temperature (20° to 25°C) for limited durations (12 hours) without significant degradation. The melting point of Acetazolamide is reported to be approximately 260.5 °C, which suggests that degradation may occur at elevated temperatures beyond this point. The stability data indicates that Acetazolamide does not decompose if used according to specifications, and no specific ignition or decomposition temperatures are provided in the safety data sheets. The absence of detailed degradation temperature data highlights the need for further studies to establish precise thermal stability parameters for Acetazolamide under various conditions. For more information, refer to the following sources: [ChemicalBook](https://www.chemicalbook.com/ChemicalProductProperty\_EN\_CB0430959.htm), [Drugs.com](https://www.drugs.com/pro/acetazolamide.html), [Cayman Chemical](https://cdn.caymanchem.com/cdn/msds/21218m.pdf), [IJPER](https://ijper.org/article/doi/6673/).  The glass transition temperature (Tg) of Acetazolamide is determined primarily using Differential Scanning Calorimetry (DSC), which is favored for its ease of use and rapid measurement capabilities. The Tg values can vary based on the heating rate; for instance, a heating rate of 10 °C/min is commonly used to ensure reproducibility. Studies indicate that the Tg of Acetazolamide is approximately 55 °C, with variations noted depending on the specific measurement technique employed, such as Dynamic Mechanical Thermal Analysis (DMTA) and Temperature Modulated DSC (TMDSC). The Tg is critical for understanding the material's thermal behavior, influencing its stability and processing conditions. The glass transition is characterized by a significant change in heat capacity, which can be quantitatively assessed through the DSC heat flow curve. The importance of standardizing measurement conditions, including cooling and heating rates, is emphasized to achieve consistent Tg values across different studies (Mazurin Gankin, 2007; Hutchinson, 2009; Rahman et al., 2007). For further details, refer to the following sources: [Glass Properties](https://glassproperties.com/tg/), [Springer](https://link.springer.com/article/10.1007/s10973-009-0268-0), [ResearchGate](https://www.researchgate.net/publication/278719107\_Determination\_of\_the\_Glass\_Transition\_by\_DSC\_A\_Comparison\_of\_Conventional\_and\_Dynamic\_Techniques).  **Boiling point:** Información no disponible |

| 1. **ANNEXES** | |
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| **ANNEX** | **DESCRIPTION** |
| 1 | IHL-42X formulation brief August 2021 |

| 1. **RELATED DOCUMENTS** | |
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| **CODE** | **DESCRIPTION** |
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| 1. **AUTHORIZATIONS** |

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| **PERFORMED BY:** | | | **REVIEWED BY:** | | | **APPROVED BY:** | |
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