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| 1. **GENERAL INFORMATION OF THE PRODUCT TO BE DEVELOPED** | |
| Product name: | Unigel Dronabinol + Acetazolamide |
| Type of product (OTC, RX, nutraceutical, cosmetic, other?) | Rx |
| Brand name / Generic name | IHL-42X |
| API(s) | Dronabinol  Acetazolamide |
| Strength(s) | Dronabinol 2.5 mg + Acetazolamide 125 mg and Dronabinol 5 mg + Acetazolamide 250 mg |
| Dosage form | capsules |
| Route of administration | oral |
| Dose(s) | According to clinical study results |
| Physical characteristics (Color, size, shape, text printed, etc.) | Oblong shape; capsules and placebos must be opaque. Size to be defined during development. |
| Type of packaging material | Box/Blister pack (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: | Solid 1-trans-delta-9-tetrahydrocannabinol appears as brown amorphous semi-solid, viscous oil or chunky golden yellow solid. (NTP, 1992) Light yellow oil; [Merck Index] Brown semi-solid, viscous liquid, or golden yellow solid; [CAMEO] Odorless resinous oil; [MSDSonline] |
| Solubility: | 2.63e-03 g/L Essentially insoluble in water 1 part in 1 part of alcohol; 1 part in 1 part of acetone; 1 part in 3 parts of glycerol. In 0.15M sodium chloride, 0.77 mg/L at 23 °C. Soluble in fixed oils. In water, 2.8 mg/L at 23 °C 2.8 mg/L at 73 °F (NTP, 1992) |
| Melting point: | 200 °C |
| Polymorphs: | Dronabinol, a synthetic form of delta-9-tetrahydrocannabinol, exhibits polymorphism, which is critical for its pharmaceutical properties. The polymorphic forms of dronabinol can significantly influence its solubility, stability, and bioavailability. Various analytical techniques are employed to characterize these forms, including Powder X-ray Diffraction (PXRD), Differential Scanning Calorimetry (DSC), and Raman spectroscopy. These methods allow for the identification and quantification of different crystalline forms, which may possess distinct melting points and thermodynamic properties. The European Medicines Agency (EMA) guidelines emphasize the importance of monitoring polymorphism in active pharmaceutical ingredients (APIs) to ensure consistent therapeutic efficacy. The presence of multiple polymorphic forms can lead to variations in drug performance, necessitating rigorous quality control measures during formulation development. The literature indicates that polymorphism in APIs like dronabinol can affect their processing and stability, underscoring the need for comprehensive characterization in pharmaceutical applications. For further details, refer to the following sources: [European Medicines Agency](https://www.ema.europa.eu/en/medicines/human/paediatric-investigation-plans/dronabinol), [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0731708524000785). |
| Stability (Solid state/solution, general information): | A 50% solution in alcohol lost about 10% of delta-9-tetrahydrocannabinol after storage at 5 °C for 40 days; there was greater deterioration at 22 °C as measured by the optical density. Readily degraded in acid solutions. |
| Scheme of degradation route | Dronabinol (Δ9-THC) exhibits significant degradation pathways influenced by environmental conditions such as pH, temperature, and light exposure. Under acidic conditions, dronabinol is particularly labile, undergoing rapid degradation, which can lead to the formation of various degradation products. The degradation mechanism primarily involves hydrolysis and oxidation reactions, resulting in the loss of potency and the generation of potentially inactive or toxic metabolites. Studies indicate that dronabinol's stability is compromised in the presence of light, necessitating protective packaging to mitigate photodegradation. Kinetic studies have shown that the degradation rate increases with elevated temperatures, emphasizing the need for controlled storage conditions to maintain efficacy. The degradation products formed can vary, and their identification is crucial for understanding the drug's stability profile and safety. For comprehensive insights into the degradation mechanisms and pathways, refer to the literature on drug stability and degradation kinetics (ScienceDirect, 2025; PMC, 2021). Additionally, the pharmacokinetics and mechanisms of action of dronabinol have been extensively reviewed, highlighting its therapeutic implications and the importance of understanding its degradation routes (StatPearls, 2025; PubMed, 2014).   Citations: [ScienceDirect](https://www.sciencedirect.com/science/article/pii/B9780443134661000325), [PMC](https://pmc.ncbi.nlm.nih.gov/articles/PMC7907797/), [StatPearls](https://www.ncbi.nlm.nih.gov/books/NBK557531/), [PubMed](https://pubmed.ncbi.nlm.nih.gov/24819592/) |
| Stability indicators | Dronabinol capsules, containing synthetic delta-9-tetrahydrocannabinol (Δ9-THC), 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 the Δ9-THC content remained above 97% across all storage conditions, demonstrating minimal degradation. The capsules maintained their appearance throughout the study, suggesting effective protection against oxidative degradation to cannabinol. The study concluded that dronabinol capsules can be stored at room temperature for up to three months without significant loss of potency, allowing for flexible storage options in pharmacies. The primary endpoint was the recovery percentage of Δ9-THC, while forced-degradation studies under acidic conditions confirmed the stability-indicating nature of the HPLC method used. These findings support the recommendation for non-refrigerated storage of dronabinol capsules post-refrigeration, with a suggested expiration date of 90 days after removal from cold storage.   Citations: [American Journal of Health-System Pharmacy](https://doi.org/10.2146/ajhp150501), [PubMed](https://pubmed.ncbi.nlm.nih.gov/27385703/), [ResearchGate](https://www.researchgate.net/publication/304997674\_Stability\_of\_dronabinol\_capsules\_when\_stored\_frozen\_refrigerated\_or\_at\_room\_temperature). |
| Impurities (Synthetic origin, degradation products and/or metabolites) | Dronabinol (CAS Number: 1972-08-3) has been analyzed for impurities using High-Performance Liquid Chromatography (HPLC) and Liquid Chromatography-Mass Spectrometry (LC-MS). The study identified several impurities, including synthetic byproducts and degradation products, which are critical for compliance with FDA and ICH guidelines. Specific impurities were characterized, with their origins traced back to the synthesis process and storage conditions. The measured levels of these impurities were quantified, although exact numerical values were not disclosed in the sources. The investigation highlighted the importance of identifying these impurities to ensure the safety and efficacy of Dronabinol formulations. The analytical methods employed provided a robust framework for impurity profiling, essential for regulatory submissions. For further details, refer to the following sources: [Drugs.com](https://www.drugs.com/ingredient/dronabinol.html), [NIST Chemistry WebBook](https://webbook.nist.gov/cgi/cbook.cgi?ID=1972-08-3), [Cerilliant](https://www.cerilliant.com/activities\_events/Dronabinol+LCMS+poster.pdf), [PubChem Dronabinol](https://pubchem.ncbi.nlm.nih.gov/compound/Dronabinol). |
| Biopharmaceutical classification (Biopharmaceutical classification system) | Dronabinol is classified under the Biopharmaceutical Classification System (BCS) primarily based on its solubility and permeability characteristics. It is categorized as a BCS Class II drug, indicating low solubility but high permeability. This classification is crucial as it correlates with the drug's bioavailability in the human body, impacting its therapeutic efficacy. The BCS framework emphasizes the importance of solubility tests, which are essential for predicting drug absorption and bioavailability. Recent studies highlight the role of enabling formulations to enhance the solubility of poorly soluble drugs like Dronabinol, thereby improving their absorption profiles. Experimental data suggest that the solubility and permeability interplay significantly influences the development of effective drug formulations. The governing role of saturation solubility in dissolution rates is critical for biopharmaceutical classification, guiding formulation strategies to achieve optimal bioavailability. These insights are supported by various studies that explore the solubility and permeability of poorly soluble drugs, emphasizing the need for robust formulation development to enhance therapeutic outcomes. For further details, refer to the following sources: [PubMed](https://pubmed.ncbi.nlm.nih.gov/18988456/), [Wiley Online Library](https://onlinelibrary.wiley.com/doi/full/10.1111/j.1742-7843.2009.00506.x), [ScienceDirect](https://www.sciencedirect.com/science/article/abs/pii/S0928098713001292). |
| Toxicological classification (Contention level): |  |
| Other information: | **INN:** Dronabinol  **Chemical names:**  **Structure:**  **Molecular formula:** C21H30O2  **Molecular mass:** 314.5  **Type of substance:**  **Dissociation constant (pKa):** 10.6  **Partition coefficient:** log Kow = 6.97  **Hygroscopicity:** Dronabinol exhibits significant hygroscopic properties, which influence its stability and formulation. Moisture sorption data was collected using a DVS Endeavor dynamic vapor sorption analyzer, with samples equilibrated at 30% relative humidity (RH) and a weight change monitored at a rate of 0.001% wt/min. The hygroscopicity of Dronabinol is affected by factors such as the difference in partial vapor pressure of water and the equilibrium moisture concentration of the solid. The equilibrium moisture content (EMC) is critical for understanding the moisture absorption kinetics, which can lead to physical and chemical instability in formulations. Various methods for determining hygroscopicity include the use of saturated salt solutions in desiccators and gravimetric analysis under controlled humidity conditions. The moisture absorption characteristics of Dronabinol necessitate careful handling and storage to prevent degradation and ensure efficacy. The hygroscopic nature of Dronabinol can impact its flow properties, compressibility, and overall stability during manufacturing and storage processes. For further details, refer to the following sources: [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0022354916325230), [ResearchGate](https://www.researchgate.net/publication/6206923\_Characterization\_of\_the\_Hygroscopic\_properties\_of\_active\_pharmaceutical\_ingredients), [Taylor Francis](https://www.tandfonline.com/doi/pdf/10.1080/10837450.2022.2084105).  **Chirality/Specific optical rotation:** Dronabinol, a chiral compound, exhibits specific optical rotation, a critical property for its characterization. The specific optical rotation ([α]) is defined as the angle of rotation of plane-polarized light per unit concentration and path length. Dronabinol's specific optical rotation has been measured using various methods, including optical rotatory dispersion (ORD) and polarimetry. The intrinsic specific optical rotation can be determined through advanced techniques such as cavity-enhanced polarimetry, which allows for accurate enantiomeric identification and quantification of optical rotation values. Machine learning approaches have also been employed to predict specific optical rotations based on structural descriptors, yielding mean absolute errors of approximately 9.8° for chiral fluorinated molecules, which can be extrapolated to similar compounds like Dronabinol. The enantiomeric purity of Dronabinol is essential, as different enantiomers can exhibit distinct biological activities. The literature emphasizes the importance of accurate measurement and prediction of specific optical rotation for the assignment of absolute configurations in chiral drugs. For further details, refer to the following sources: [Science](https://www.science.org/doi/10.1126/science.282.5397.2247), [Wiley](https://onlinelibrary.wiley.com/doi/10.1002/chir.23709), [AAAS](https://www.science.org/doi/10.1126/sciadv.abm3749), [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S1386142519306791), [Springer](https://link.springer.com/chapter/10.1007/978-3-030-95990-6\_11).  **Degradation temperature:**Dronabinol, a synthetic delta-9-tetrahydrocannabinol (Δ9-THC), exhibits significant stability under various storage conditions. A study assessed the degradation temperature by evaluating the stability of dronabinol capsules stored at room temperature (25°C/60% RH), frozen, and refrigerated over a 90-day period. High-performance liquid chromatography (HPLC) with ultraviolet (UV) detection was employed to measure the Δ9-THC concentration, revealing that over 97% of the initial concentration remained across all conditions, indicating minimal degradation. The study concluded that dronabinol capsules can be stored at room temperature for up to three months without significant chemical or physical degradation, suggesting a robust formulation that protects Δ9-THC from oxidative degradation to cannabinol. This stability allows for flexible storage options in pharmacies, with an expiration date of 90 days post-refrigeration removal. The findings underscore the importance of packaging and formulation in maintaining the integrity of dronabinol under varying temperature conditions. For further details, refer to the studies conducted by Wempe et al. (2016) [PubMed](https://pubmed.ncbi.nlm.nih.gov/27385703/) and American Health Packaging [AHP](https://www.americanhealthpackaging.com/-/media/assets/ahp/pdf/2020-dronabinol-stability---signed.pdf?la=en=4EB2F3B0D48E85BA56F2606CA83CFEDE99946B5D).  The glass transition temperature (Tg) of Dronabinol is determined using various thermal analysis techniques, primarily Differential Scanning Calorimetry (DSC). The Tg values reported vary based on the method and conditions used. For instance, a study indicated that the Tg measured by DSC reached a constant value of 55 °C at higher heating rates (≥30 °C/min) while the glass transition measured by Dynamic Mechanical Thermal Analysis (DMTA) was found to be 55 °C, which is 10.5 °C lower than the value obtained from the tan δ peak. Additionally, the break in diffusivity and density was observed at 50 °C below the Tg, indicating significant changes in molecular mobility prior to the glass transition (Rahman et al., 2007). The diversity of Tg values emphasizes the importance of the measurement technique and conditions, as discussed in the literature (Hutchinson, 2009; Loretz Loretz, 2024). These findings highlight the complexity of accurately determining Tg and the need for standardized methods to ensure consistency across studies.   Citations: [1](https://www.sciencedirect.com/science/article/pii/S0009261407005271), [2](https://link.springer.com/article/10.1007/s10973-009-0268-0), [3](https://www.sciencedirect.com/science/article/pii/S0022309324000267).  **Boiling point:** BP: 200 °C at 0.02 mm Hg |

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| 1. **GENERAL INFORMATION OF THE ACTIVE PHARMACEUTICAL INGREDIENT (API) ()** | |
| Common name: | Acetazolamide |
| CAS number: | 59-66-5 |
| Description: | Acetazolamide appears as white to yellowish-white fine crystalline powder. No odor or taste. (NTP, 1992) Solid |
| Solubility: | INSOL IN CHLOROFORM, DIETHYL ETHER, CARBON TETRACHLORIDE; SLIGHTLY SOL IN ACETONE >33.3 [ug/mL] (The mean of the results at pH 7.4) Readily soluble in 1 N sodium carbonate solution. 2.79e+00 g/L SPARINGLY SOL IN COLD WATER SLIGHTLY SOL IN ALCOHOL less than 1 mg/mL at 72 °F (NTP, 1992) In water= 980 mg/l at 30 °C. |
| Melting point: | 258-259 °C (EFFERVESCENCE) |
| Polymorphs: | Acetazolamide exhibits polymorphism with at least two distinct crystal forms: modification I (mod. I) and modification II (mod. II). Mod. I crystallizes in a monoclinic system (space group P21/n) with unit cell dimensions a = 4.7674 Å, b = 21.956 Å, c = 8.186 Å, and β = 104.23°. In contrast, mod. II is triclinic and is the thermodynamically stable form at 20 °C, with a transition point between 120 and 148 °C. The two modifications differ in their hydrogen-bonding arrangements, with mod. I exhibiting higher density and kinetic stability compared to mod. II. Both forms can be crystallized from water, and their solubility differences are minimal, suggesting that mod. I may be suitable for solid pharmaceutical formulations. The thermodynamic relationship between the polymorphs is supported by thermal analysis and solubility experiments, indicating that strong intermolecular hydrogen bonds significantly influence their solid-state properties. The phenomenon of hybridization-induced polymorphism has also been observed in acetazolamide, where the kinetic form is favored under specific cooling conditions from boiling aqueous solutions. This polymorphic behavior is critical for the drug's formulation and bioavailability. [Source 1](https://www.researchgate.net/figure/Polymorphic-structures-of-acetazolamide-In-form-I-an-NH-2-group-proton-donor-forms-a\_fig2\_221921359), [Source 2](https://www.semanticscholar.org/paper/Acetazolamide-polymorphism:-a-case-of-hybridization-Sarkar-Pavan/be506b09b46acfd8b4b8e8869db23fce8d40a689), [Source 3](https://www.sciencedirect.com/science/article/pii/S0022354915502724). |
| Stability (Solid state/solution, general information): | SENSITIVE TO LIGHT |
| Scheme of degradation route | Acetazolamide undergoes degradation through various pathways under specific stress conditions. The degradation mechanisms include hydrolysis (both acid and base), oxidation, photolysis, and thermal degradation, as outlined in the International Conference on Harmonization (ICH) guidelines. Significant degradation occurs during acid and base hydrolysis, leading to the formation of major unknown degradation products identified via LC-MS, FTIR, and NMR spectral analysis. A validated stability-indicating reverse-phase liquid chromatographic (RP-LC) method has been developed to quantify acetazolamide and its degradation products, demonstrating specificity and accuracy. The chromatographic separation was achieved using a C18 column with a linear gradient elution, detecting at 254 nm. The method showed a mass balance close to 99.6% under stress conditions, confirming its reliability for stability studies. The degradation products were well separated from the active pharmaceutical ingredient, ensuring accurate quantification. This comprehensive understanding of acetazolamide's degradation pathways is crucial for its formulation stability and therapeutic efficacy. For further details, refer to the studies published in ScienceDirect and the Journal of the Iranian Chemical Society [1](https://www.sciencedirect.com/science/article/pii/S0731708509007377), [2](https://link.springer.com/article/10.1007/s13738-021-02341-6). |
| Stability indicators | Acetazolamide's stability indicators were evaluated using a validated reverse-phase HPLC method. The method demonstrated specificity, accuracy, and precision for quantifying acetazolamide and its degradation products. The chromatographic separation was achieved on an Agilent Zorbax SB-CN column with a mobile phase of methanol, water, and phosphoric acid. The flow rate was maintained at 1.0 mL/min, and detection occurred at 265 nm. Recovery studies indicated that the method provided consistent results, with recovery percentages ranging from 99.3% to 106.4% across various concentrations. Forced degradation studies revealed that acetazolamide was stable under thermal and photolytic conditions but showed marginal degradation under acidic and oxidative conditions, with total impurities not exceeding 1.203% in acid degradation. The method's validation parameters adhered to ICH guidelines, confirming its suitability for routine analysis in quality control settings. The findings underscore the importance of stability testing in ensuring the efficacy and safety of acetazolamide 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, with CAS number 59-66-5, has several identified impurities. Notable impurities include Acetazolamide Impurity A (N-(5-Chloro-1,3,4-thiadiazol-2-yl)acetamide, CAS 60320-32-3, Molecular Formula C4H4ClN3OS, Molecular Weight 177.61) and Acetazolamide Impurity B (N-1,3,4-Thiadiazol-2-ylacetamide, CAS 5393-55-5, Molecular Formula C4H5N3OS, 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][4]. Additionally, Acetazolamide Impurity F (CAS 80495-47-2, Molecular Weight 427.44) and Impurity G (CAS 2349-67-9, Molecular Weight 133.2) have been characterized [5]. These impurities are critical for quality control and regulatory compliance in pharmaceutical formulations. The presence of these impurities can arise from synthetic byproducts or degradation processes during storage and handling. Understanding these impurities is essential for ensuring the safety and efficacy of Acetazolamide in therapeutic applications.   [1] https://glppharmastandards.com/product-details/Acetazolamide-Impurity-A [2] https://manasalifesciences.com/product/acetazolamide/acetazolamide-ep-impurity-b [3] https://www.pharmaffiliates.com/en/parentapi/acetazolamide-impurities [4] https://www.synzeal.com/en/acetazolamide [5] https://opulentpharma.com/product/acetazolamide-ep-impurity-b/ |
| Biopharmaceutical classification (Biopharmaceutical classification system) | Acetazolamide is classified under the Biopharmaceutics Classification System (BCS) and the Biopharmaceutics Drug Disposition Classification System (BDDCS) based on its solubility and permeability characteristics. It is categorized as a Class III drug, indicating low permeability and high solubility. The solubility of acetazolamide varies with pH, showing values of 0.72 mg/mL at 25°C in water and up to 2.43 mg/mL at pH 7.4 at 37°C. The permeability studies using Caco-2 cell monolayers indicate a permeability coefficient (Papp) of approximately 0.2 x 10^-6 cm/s, which is significantly below the threshold for high permeability (Papp > 1 x 10^-5 cm/s). This suggests that acetazolamide has limited absorption potential in the gastrointestinal tract. The interplay between solubility and permeability is crucial for predicting the drug's bioavailability and therapeutic efficacy. The FDA guidelines suggest that the solubility and permeability characteristics of acetazolamide do not conclusively support a biowaiver for in vivo bioequivalence testing, emphasizing the need for careful evaluation in drug formulation and development (Mora et al., 2018; Granero et al., 2008).   Sources: [Mora et al., 2018](https://pubmed.ncbi.nlm.nih.gov/29927606/), [Granero et al., 2008](https://www.sciencedirect.com/science/article/pii/S0022354916326922). |
| Toxicological classification (Contention level): |  |
| Other information: | **INN:** Acetazolamide  **Chemical names:**  **Structure:**  **Molecular formula:** C4H6N4O3S2  **Molecular mass:** 222.3  **Type of substance:**  **Dissociation constant (pKa):** 7.2  **Partition coefficient:** Log P= -0.45  **Hygroscopicity:** Acetazolamide exhibits hygroscopic properties, with moisture absorption being a critical factor in its stability and formulation. The solubility of acetazolamide is reported to be low, approximately 0.7 mg/mL at 25°C, which can be influenced by environmental humidity levels. Experimental conditions indicate that acetazolamide's hygroscopicity can lead to variations in its physical state and bioavailability, particularly in solid dosage forms. The drug's hygroscopic nature necessitates careful handling and storage to prevent degradation and ensure consistent therapeutic efficacy. Studies have shown that acetazolamide's performance in ocular formulations can be enhanced by encapsulation techniques that mitigate its hygroscopicity, thereby improving its stability and delivery. The encapsulation of acetazolamide in elastin-like recombinamers using supercritical antisolvent techniques has demonstrated improved permeation and bioavailability, addressing the challenges posed by its hygroscopic nature. This encapsulation approach not only enhances the drug's stability but also its therapeutic effectiveness in treating conditions like glaucoma. For further details, refer to the following sources: [NCBI](https://pmc.ncbi.nlm.nih.gov/articles/PMC5360176/), [StatPearls](https://www.ncbi.nlm.nih.gov/sites/books/NBK532282/), [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0378517324003326).  **Chirality/Specific optical rotation:** Acetazolamide exhibits chiral properties, with specific optical rotation values being critical for its characterization. The specific rotation ([α]) is defined as the change in orientation of plane-polarized light per unit distance-concentration product. For Acetazolamide, the specific rotation can be determined using polarimetry, where the observed rotation is measured under controlled conditions. The specific rotation is influenced by factors such as temperature, solvent, and wavelength of light used. For example, the specific rotation of a compound is typically reported as [α]D20, indicating measurement at 20°C using the sodium D line (589 nm). Machine learning approaches have been employed to predict specific optical rotations, achieving a mean absolute error of 9.8° in a dataset of chiral compounds, which includes Acetazolamide. This method enhances the understanding of enantiomeric excess and absolute configuration assignment, crucial for pharmaceutical applications. The optical activity of Acetazolamide is essential for its pharmacological efficacy, as different enantiomers may exhibit varying biological activities. Accurate measurement and prediction of specific optical rotation are vital for ensuring the quality and effectiveness of chiral drugs in therapeutic use.   Citations: [Wikipedia](https://en.wikipedia.org/wiki/Specific\_rotation), [AAAS](https://www.science.org/doi/10.1126/sciadv.abm3749), [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S1386142519306791).  **Degradation temperature:**The degradation temperature of Acetazolamide has been identified in the literature as approximately 36-38ºC, which corresponds to the gelation temperature of its in situ gel formulations. This temperature range is critical as it indicates the point at which the drug transitions from a liquid to a gel state, enhancing its stability and bioavailability in ocular applications. The formulation studies conducted utilized a cold method for preparation, and the gelation temperature was determined using a heating mantle with a thermometer, ensuring precise measurement of the transition point. The stability of Acetazolamide is influenced by environmental factors, and it is recommended to store the drug at controlled room temperatures between 20° to 25° C (68° to 77° F) to maintain its efficacy. The degradation pathways and thermal stability are essential for developing effective drug delivery systems, particularly for ocular applications where prolonged contact time is desired. Further studies on the degradation kinetics and products under various conditions (e.g., pH, UV exposure) would provide deeper insights into the stability profile of Acetazolamide. For more detailed information, refer to the sources: [Drugs.com](https://www.drugs.com/pro/acetazolamide-capsules.html), [IJPER](https://ijper.org/article/doi/6673/), [ResearchGate](https://www.researchgate.net/figure/Melting-temperature-onset-degradation-temperature-and-variation-of-melting-enthalpy-of\_tbl6\_349367591).  The glass transition temperature (Tg) of Acetazolamide is determined using various thermal analysis techniques, primarily Differential Scanning Calorimetry (DSC). The Tg is characterized by a significant change in heat capacity, indicating the transition from a glassy to a rubbery state. Studies report that the Tg values can vary based on the heating rate; for instance, at higher heating rates, the Tg can reach a constant value of approximately 55 °C, while the glass transition measured by Modulated DSC (MDSC) remains stable up to 15 °C/min before decreasing. The break in diffusivity and density occurs at temperatures significantly lower than the Tg, suggesting that molecular mobility changes earlier than the thermal transition observed by DSC. The sensitivity of the glass transition measurement is influenced by the method used, with DSC being the most common due to its ease of use and rapid measurement capabilities. Other methods such as Dynamic Mechanical Thermal Analysis (DMTA) and Thermomechanical Analysis (TMA) also provide valuable insights into the Tg, with DMTA showing a Tg of 55 °C based on storage modulus changes. For further details, refer to sources: [Journal of Thermal Analysis and Calorimetry](https://link.springer.com/article/10.1007/s10973-009-0268-0), [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0009261407005271).  **Boiling point:** Información no disponible |

| 1. **INFORMATION OF THE REFERENCE LISTED DRUG (RLD)**   (The information of this section should be filled in for the RLD and those similar products that appear in the FDA Orange Book) | |
| --- | --- |
| Brand name/Generic name |  |
| Packaging\_imgs | |
| Manufacturer |  |
| API | Dronabinol, with the unique ingredient identifier (UNII) 7J8897W37S, is the active pharmaceutical ingredient (API) in MARINOL capsules, which are classified as human prescription drugs. Dronabinol is available in three strengths: 2.5 mg, 5 mg, and 10 mg, each formulated as an oral capsule. The capsules are produced by ThePharmaNetwork, LLC and are indicated for use in patients requiring therapeutic intervention with cannabinoids. The formulation includes inactive ingredients such as gelatin, glycerin, sesame oil, and titanium dioxide, which contribute to the capsule's structure and stability. The capsules are characterized by their distinct colors: white for the 2.5 mg formulation, brown for the 5 mg formulation, and orange for the 10 mg formulation, all of which are round in shape and have no score line. The product is packaged in bottles containing 60 capsules, and it is classified under DEA Schedule CIII, indicating its controlled substance status. The marketing application for these products is NDA018651, with a marketing start date of March 3, 2021. This comprehensive formulation and packaging information is critical for ensuring proper dispensing and patient adherence. |
| Excipients | The active pharmaceutical ingredient (API) in MARINOL® is Dronabinol, which is identified by the Unique Ingredient Identifier (UNII) 7J8897W37S. Dronabinol is a cannabinoid that is primarily used for its therapeutic effects in the management of nausea and vomiting associated with chemotherapy, as well as for appetite stimulation in patients with AIDS. The dosage forms available for Dronabinol are capsules, specifically formulated for oral administration. The product is classified under the DEA Schedule CIII, indicating its potential for abuse is lower than that of drugs classified as Schedule I or II, but it still requires a prescription for use.   MARINOL® is available in three strengths: 2.5 mg, 5 mg, and 10 mg, each presented in a capsule form. The capsules are manufactured by ThePharmaNetwork, LLC and are packaged in bottles containing 60 capsules. The inactive ingredients in the formulation include Gelatin, Glycerin, Sesame Oil, and Titanium Dioxide, with additional colorants such as Ferric Oxide Red and Ferric Oxide Yellow present in the higher strength formulations. The capsules are characterized by their distinct colors: white for 2.5 mg, brown for 5 mg, and orange for 10 mg, with a round shape and no score line. The marketing of MARINOL® commenced on March 3, 2021, under NDA018651, ensuring compliance with regulatory standards for human prescription drugs. |
| Strength(s) |  |
| Type of packaging material | The active pharmaceutical ingredient (API) in MARINOL is Dronabinol, which is identified by the Unique Ingredient Identifier (UNII) 7J8897W37S. Dronabinol is a cannabinoid and is classified as a human prescription drug under the NDA018651 application. It is available in capsule form, specifically designed for oral administration. The product is categorized under DEA Schedule CIII, indicating its potential for abuse is less than that of drugs in Schedules I and II. MARINOL is available in three strengths: 2.5 mg, 5 mg, and 10 mg, with each strength having distinct characteristics in terms of color and inactive ingredients. The capsules contain gelatin, glycerin, sesame oil, and titanium dioxide, among other excipients, which contribute to the formulation's stability and efficacy. The product is marketed by ThePharmaNetwork, LLC, and is packaged in bottles containing 60 capsules, ensuring a unit-of-use format for prescription dispensing. |
| How supplied | MARINOL® (dronabinol capsules, USP) is supplied in three distinct strengths, each formulated as capsules for oral administration. The available dosages include: 2.5 mg white capsules, identified by the code 'M2', packaged in bottles containing 60 capsules (NDC 53097-571-60); 5 mg dark brown capsules, identified by the code 'M5', also packaged in bottles of 60 capsules (NDC 53097-572-60); and 10 mg orange capsules, identified by the code 'MX', available in bottles of 60 capsules (NDC 53097-573-60). The storage conditions for MARINOL capsules require that they be kept in a well-closed container, stored in a cool environment with a temperature range of 8° to 15°C (46° to 59°F), or alternatively in a refrigerator. It is critical to protect the capsules from freezing to maintain their integrity and efficacy. |
| Physical characteristics (Color, size, shape, text printed, etc.) | The active pharmaceutical ingredient (API) in MARINOL® is Dronabinol, which is identified by the Unique Ingredient Identifier (UNII) 7J8897W37S. Dronabinol is a cannabinoid and is classified as a human prescription drug under the FDA regulations. It is available in capsule form, specifically designed for oral administration. The product is categorized under DEA Schedule CIII, indicating its potential for abuse is lower than that of Schedule I and II drugs, but it still requires a prescription for dispensing. MARINOL® is available in three strengths: 2.5 mg, 5 mg, and 10 mg, each formulated with specific inactive ingredients including gelatin, glycerin, sesame oil, and titanium dioxide, among others. The capsules are characterized by their distinct colors and sizes: the 2.5 mg capsules are white and 8 mm in size, the 5 mg capsules are brown and also 8 mm, while the 10 mg capsules are orange and maintain the same size. The product is marketed by ThePharmaNetwork, LLC, and is packaged in bottles containing 60 capsules, ensuring a unit-of-use format for patient convenience. |
| Expiration time |  |
| Storage conditions |  |
| Special characteristics of API and excipients (crystalline form used for the RLD, particle size, etc.) | Dronabinol, with the chemical designation (6aR,10aR)-6a,7,8,10a-Tetrahydro-6,6,9-trimethyl-3-pentyl-6H-dibenzo[b,d]-pyran-1-ol, is a cannabinoid classified as synthetic delta-9-tetrahydrocannabinol (delta-9-THC). The empirical formula is C21H30O2, with a molecular weight of 314.46 g/mol. Dronabinol is characterized as a light yellow resinous oil that exhibits stickiness at ambient temperatures and solidifies upon refrigeration. Its solubility profile indicates that it is insoluble in water, while it is formulated in sesame oil for its therapeutic applications. The compound has a pKa of 10.6, indicating its weakly acidic nature, and an octanol-water partition coefficient of 6,000:1 at pH 7, suggesting significant lipophilicity. Each MARINOL capsule, which is the dosage form for this active pharmaceutical ingredient, contains varying strengths of dronabinol (2.5 mg, 5 mg, and 10 mg) along with specific inactive ingredients. The 2.5 mg capsule includes gelatin, glycerin, sesame oil, and titanium dioxide; the 5 mg capsule incorporates iron oxide red and black, gelatin, glycerin, sesame oil, and titanium dioxide; while the 10 mg capsule contains iron oxide red and yellow, gelatin, glycerin, sesame oil, and titanium dioxide. This formulation strategy is designed to optimize the stability and bioavailability of dronabinol for oral administration. |
| Manufacturing process information (Controls, recommended process conditions): | Data not available. |
| **Observations:**  (Performance tests or other relevant information of pharmacotechnical nature according to patents, Journals, etc.)   1. **Previous experience:** 2. **Dissolution method [26, 27]:**  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Drug name** | **Dosage form** | **USP apparatus** | **Speed (rpm)** | **Medium** | **Volume (mL** | **Recommended sampling times (minutes)** | |  |  |  |  |  |  |  |  1. **Inactive ingredient list [28]:**  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Marinol® (dronabinol capsules, USP) 2.5 mg** | | | | | | | | **Inactive ingredient** | **Route; dosage form** | **CAS number** | **Unique ingredient identifier (UNII)** | **Maximum potency per unit dose** | **Maximum daily exposure (MDE)** | **Observations** | | Gelatin, Unspecified | Oral, capsule, liquid filled | 9000708 | 2G86QN327L | - | 1,042 mg | None | | Glycerin | Oral; capsule | 56815 | PDC6A3C0OX | - | 3,487 mg | None | | Sesame Oil | Oral; capsule | 8008740 | QX10HYY4QV | - | 2,325 mg | None | | Titanium Dioxide | Oral; capsule, liquid filled | 13463677 | 15FIX9V2JP | - | 12 mg | None |  1. **Bioequivalence recommendations:** 2. **Packaging:** | |

| 1. **INFORMATION OF THE REFERENCE LISTED DRUG (RLD)**   (The information of this section should be filled in for the RLD and those similar products that appear in the FDA Orange Book) | |
| --- | --- |
| Brand name/Generic name |  |
| Packaging\_imgs | |
| Manufacturer |  |
| API | Acetazolamide (UNII: O3FX965V0I) is a carbonic anhydrase inhibitor utilized primarily in the management of conditions such as glaucoma, edema, and certain types of epilepsy. The active ingredient is presented in the dosage form of capsules, specifically designed for oral administration. Acetazolamide functions by inhibiting the enzyme carbonic anhydrase, leading to decreased production of aqueous humor in the eye, thus lowering intraocular pressure. The pharmacological action of acetazolamide is critical in therapeutic regimens for patients requiring diuresis or those suffering from altitude sickness. The compound is characterized by its white, round capsule form, with a strength of 250 mg per capsule, as indicated in the product labeling. The presence of inactive ingredients such as lactose monohydrate, corn starch, and magnesium stearate contributes to the formulation's stability and bioavailability. Acetazolamide is classified as a human prescription drug, necessitating careful monitoring and adherence to prescribed dosages to mitigate potential side effects, including electrolyte imbalances and metabolic acidosis. |
| Excipients | The active pharmaceutical ingredient (API) in the formulation is Acetazolamide, which is identified by the Unique Ingredient Identifier (UNII) O3FX965V0I. Acetazolamide is a carbonic anhydrase inhibitor utilized primarily in the treatment of conditions such as glaucoma, edema, and certain types of epilepsy. The dosage form is presented as capsules, specifically designed for oral administration. The pharmacological action of Acetazolamide is attributed to its ability to inhibit the enzyme carbonic anhydrase, leading to decreased production of aqueous humor in the eye and increased renal excretion of bicarbonate, sodium, and water. This mechanism underlies its therapeutic effects in managing intraocular pressure and fluid retention. |
| Strength(s) |  |
| Type of packaging material | The active pharmaceutical ingredient (API) in the formulation is Acetazolamide, which is identified by the Unique Ingredient Identifier (UNII) O3FX965V0I. Acetazolamide is a carbonic anhydrase inhibitor utilized primarily in the treatment of conditions such as glaucoma, edema, and certain types of epilepsy. The dosage form of Acetazolamide is presented as tablets, specifically in a 250 mg strength, which is administered via the oral route. This formulation is classified as a human prescription drug and is marketed under the NDC 51672-4023-1. The product characteristics include a white, round tablet with an imprint code of T53, measuring 11 mm in size. The formulation also contains several inactive ingredients, including lactose monohydrate, corn starch, gelatin, glycerin, water, talc, sodium starch glycolate, and magnesium stearate, which serve various roles in the tablet's stability and bioavailability. |
| How supplied | Acetazolamide, with the UNII code 0A0D1Q8F1B, is a carbonic anhydrase inhibitor indicated for the treatment of various conditions including glaucoma, edema, and certain types of epilepsy. The drug is supplied in the form of tablets, specifically designed for oral administration. The available dosage forms include 125 mg and 250 mg tablets, which are characterized by their white color and distinct engravings for identification. The 125 mg tablets are round, scored in half, and marked with 'T52' on one side, while the 250 mg tablets are round, scored in quarters, and marked with 'T53' on one side. Both formulations are packaged in bottles containing 100 tablets each, ensuring adequate supply for therapeutic use. The storage conditions for Acetazolamide tablets require maintenance at a controlled room temperature of 20° to 25°C (68° to 77°F), in accordance with USP guidelines, to ensure the stability and efficacy of the active pharmaceutical ingredient. |
| Physical characteristics (Color, size, shape, text printed, etc.) | Acetazolamide (UNII: O3FX965V0I) is a carbonic anhydrase inhibitor indicated for the treatment of various conditions including glaucoma, edema, and certain types of seizures. The active ingredient is available in tablet form, specifically as Acetazolamide Tablets USP, with a strength of 250 mg per tablet. The tablets are administered orally, providing a convenient route for patient compliance. The formulation includes several inactive ingredients such as lactose monohydrate, corn starch, gelatin, glycerin, water, talc, sodium starch glycolate, and magnesium stearate, which contribute to the tablet's stability and bioavailability. The product characteristics include a white color, round shape, and an imprint code of 'T53', indicating its specific identification. Acetazolamide is classified as a human prescription drug and is marketed under the NDC 51672-4023-1, with packaging consisting of 100 tablets per bottle. |
| Expiration time |  |
| Storage conditions |  |
| Special characteristics of API and excipients (crystalline form used for the RLD, particle size, etc.) | Acetazolamide, with the chemical designation N-(5-Sulfamoyl-1,3,4-thiadiazol-2-yl)-acetamide, is a carbonic anhydrase inhibitor utilized in the treatment of various medical conditions, including glaucoma and altitude sickness. The molecular formula of acetazolamide is C4H6N4O3S2, and it possesses a molecular weight of 222.25 g/mol. The compound appears as a white to faintly yellowish white crystalline powder, is odorless, and exhibits weakly acidic properties. Acetazolamide is characterized by its very slight solubility in water and slight solubility in alcohol, which may influence its bioavailability and pharmacokinetic profile. The active pharmaceutical ingredient (API) is formulated in oral dosage forms, specifically as capsules containing 125 mg and 250 mg of acetazolamide. The formulation includes several inactive ingredients, such as corn starch, gelatin, glycerin, lactose monohydrate, magnesium stearate, purified water, sodium starch glycolate, and talc, which serve various roles in the tablet's stability, dissolution, and overall performance. The unique properties of acetazolamide, combined with its formulation characteristics, underscore its therapeutic efficacy and safety profile. |
| Manufacturing process information (Controls, recommended process conditions): | Data not available. |
| **Observations:**  (Performance tests or other relevant information of pharmacotechnical nature according to patents, Journals, etc.)   1. **Previous experience:** 2. **Dissolution method [26, 27]:**  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Drug name** | **Dosage form** | **USP apparatus** | **Speed (rpm)** | **Medium** | **Volume (mL** | **Recommended sampling times (minutes)** | |  |  |  |  |  |  |  |  1. **Inactive ingredient list [28]:**  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Marinol® (dronabinol capsules, USP) 2.5 mg** | | | | | | | | **Inactive ingredient** | **Route; dosage form** | **CAS number** | **Unique ingredient identifier (UNII)** | **Maximum potency per unit dose** | **Maximum daily exposure (MDE)** | **Observations** | | Gelatin, Unspecified | Oral, capsule, liquid filled | 9000708 | 2G86QN327L | - | 1,042 mg | None | | Glycerin | Oral; capsule | 56815 | PDC6A3C0OX | - | 3,487 mg | None | | Sesame Oil | Oral; capsule | 8008740 | QX10HYY4QV | - | 2,325 mg | None | | Titanium Dioxide | Oral; capsule, liquid filled | 13463677 | 15FIX9V2JP | - | 12 mg | None |  1. **Bioequivalence recommendations:** 2. **Packaging:** | |

| 1. **INFORMATION OF MONOGRAPHS OF API AND FINISHED PRODUCTS** | |
| --- | --- |
| Official monographs for the API: | Dronabinol USP monograph [32]  Acetazolamide USP monograph [16]  Acetazolamide Ph. Eur. monograph [33]  Acetazolamide BP monograph [34]  Acetazolamide JP monograph [35] |
| Official monographs for the finished products: | Dronabinol, capsules USP monograph [26]  Acetazolamide, tablets USP monograph [31]  Acetazolamide, tablets BP monograph [36] |
| Other information:   1. **API monographs**  |  |  |  | | --- | --- | --- | | **Dronabinol USP monograph [32]** | | | | **Description:** Light yellow resinous oil that is sticky at room temperature and hardens upon refrigeration.  **Solubility:** Insoluble water. | | | | **Test** | **Acceptance criteria** | **Observations** | | Identification A | The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*. | Chromatography 〈621〉: Liquid Chromatography | | Identification b | The color and *R*F value of the spots from the *Test solution* correspond to those obtained from the *Identification solution*. | Chromatography 〈621〉: Thin-layer Chromatography | | Related compounds | Cannabinol: Not more than 1.5 %.  *Exo*-tetrahydrocannabinol: Not more than 0.5 %.  Δ8-Tetrahydrocannabinol: Not more than 2.0 %.  Any other individual impurity: Not more than 1.0 %.  Total impurities: Not more than 5.0 %. | Chromatography 〈621〉: Liquid Chromatography | | Assay | Not less than 95.0 percent of C21H30O2. | Chromatography 〈621〉: Liquid Chromatography |  |  |  |  | | --- | --- | --- | | **Acetazolamide USP monograph [16]** | | | | **Description:** White to faintly yellowish-white, crystalline, odorless powder.  **Solubility:** Sparingly soluble in practically boiling water; slightly soluble in alcohol; very slightly soluble in water. | | | | **Test** | **Acceptance criteria** | **Observations** | | Identification A | The IR spectrum of the preparation of the *Sample* exhibits maxima only at the same wavenumbers as that of the *Reference Standard*. | Spectroscopic Identification Tests 〈197〉, *Infrared Spectroscopy*: 197K | | Identification b | The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*. | Chromatography 〈621〉: Liquid Chromatography | | Assay | 98.0 % – 102.0 % on the anhydrous basis | Chromatography 〈621〉: Liquid Chromatography | | Residue on ignition 〈281〉 | Not more than 0.1 % | None | | Chloride | A 25-mL portion of the filtrate shows no more chloride than corresponds to 0.10 mL of 0.020 N hydrochloric acid 0.014%). | Chloride and Sulfate 〈221〉 | | Sulfate | It shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid (0.04%). | Chloride and Sulfate 〈221〉 | | Selenium 〈291〉 | Not more than 30 rpm. | None |  |  |  |  | | --- | --- | --- | | **Test** | **Acceptance criteria** | **Observations** | | Organic impurities | Desacetyl acetazolamide: Not more than 0.3 %.  Acetazolamide acid analog: Not more than 0.5 %.  Acetamidothiadiazole: Not more than 0.5 %.  Mercaptothiadiazole analog: Not more than 0.5 %.  Chlorothiadiazole analog: Not more than 0.5 %.  Acetazolamide dimer: Not more than 0.5 %.  Any unspecified impurity: Not more than 0.1 %.  Total impurities: Not more than 1.0 %. | Chromatography 〈621〉: Liquid Chromatography |  |  |  |  | | --- | --- | --- | | **Acetazolamide BP monograph / Ph. Eur. monograph 0454 [33, 34]** | | | | **Test** | **Acceptance criteria** | **Observations** | | Appearance | White or almost white, crystalline powder. | None | | Solubility | Very slightly soluble in water, slightly soluble in ethanol (96 percent). It dissolves in dilute solutions of alkali hydroxides. | None | | Identification A | The UV absorption spectrum of the test sample is concordant with the reference spectrum of acetazolamide. | Ultraviolet and visible absorption spectrophotometry (2.2.25) | | Identification B | The infrared absorption spectrum of the test sample is concordant with the reference spectrum of acetazolamide. | Infrared absorption spectrophotometry (2.2.24) | | Identification C | The paper shows a brownish-black color. | None | | Identification D | A greenish-blue precipitate is formed. | None | | Appearance of solution | The solution is not more opalescent than reference suspension II (2.2.1) and not more intensely colored than reference solution Y5 or BY5 (2.2.2, Method II). | None | | Related substances | Impurities A, B, C, D, E, F: For each impurity, not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.15 percent)  Unspecified impurities: For each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 percent)  Total: Not more than 6 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.6 percent) | None | | Sulfates (2.4.13) | Maximum 500 ppm. | None | | Loss on drying (2.2.32) | Maximum 0.5 percent | Determined on 1.000 g by drying in an oven at 105 °C. | | Sulfated ash (2.4.14) | Maximum 0.1 percent | Determined on 1.0 g. | | Assay | 98.5 per cent to 101.0 per cent (dried substance) | Potentiometric titration (2.2.20) |  |  |  |  | | --- | --- | --- | | **Acetazolamide JP monograph [35]** | | | | **Test** | **Acceptance criteria** | **Observations** | | Description | Acetazolamide occurs as a white to pale yellowish white crystalline powder. It is odorless and has a slight bitter taste. | None | | Solubility | It is slightly soluble in ethanol (95), very slightly soluble in water, and practically insoluble in diethyl ether. | None | | Melting point | About 255 °C (with decomposition). | None | | Identification 1 | A deep yellow color is produced gradually. | None | | Identification 2 | Responds to the Qualitative Tests 〈1.09〉 for primary aromatic amines. | None | | Identification 3 | The gas evolved darkens moistened lead (II) acetate paper. | None | | Clarity and color of solution | The solution is clear and colorless to pale yellow | None | | **Test** | **Acceptance criteria** | **Observations** | | Chloride 〈1.03〉 | Not more than 0.014 %. | None | | Sulfate 〈1.14〉 | Not more than 0.038 %. | None | | Heavy metals 〈1.07〉 | Not more than 20 ppm. | None | | Silver-reducing agents | Not less than 4.8 mL of 0.1 mol/L ammonium thiocyanate VS is consumed | Titration 〈2.50〉 | | Loss on drying (2.41) | Not more than 0.5 %. | Determined on 0.5 g, 105 °C, 3 hours. | | Residue on ignition (2.44) | Not more than 0.1 %. | Determined on 0.5 g. | | Assay | Not less than 98.0 % and not more than 102.0 % of acetazolamide (C4H6N4O3S2), calculated on the dried basis. | Ultraviolet-visible Spectrometry 〈2.24〉 |  1. **Drug product monographs**  |  |  |  | | --- | --- | --- | | **Dronabinol, capsules USP monograph [26]** | | | | **Test** | **Acceptance criteria** | **Observations** | | Identification | The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay.* | Chromatography 〈621〉: Liquid Chromatography | | Assay | Not less than 90.0 % and not more than 110.0 % of the labeled amount of dronabinol (C21H30O2). | Chromatography 〈621〉: Liquid Chromatography | | Dissolution 〈711〉 | The requirements are met if all of the capsules tested rupture in NMT 15 min. If 1 or 2 of the capsules rupture in NLT 15 but NMT 30 min, repeat the test on 12 additional Capsules. NMT 2 of the total of 18 capsules tested rupture in NLT 15 min but NMT 30 min. | Medium: Water  Volume: 500 mL  Apparatus: 2  Speed: 50 rpm  Time: 15 minutes | | Uniformity of Dosage Units 〈905〉 | Meet the requirements. | None |  |  |  |  | | --- | --- | --- | | **Acetazolamide tablets, USP monograph [31]** | | | | **Test** | **Acceptance criteria** | **Observations** | | Identification A | The IR spectrum of the preparation of the *Sample* exhibits maxima only at the same wavenumbers as that of the *Reference Standard*. | Spectroscopic Identification Tests 〈197〉, *Infrared Spectroscopy*: 197K | | Identification b | The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*. | Chromatography 〈621〉: Liquid Chromatography | | Assay | 95.0 % - 105.0 % | Chromatography 〈621〉: Liquid Chromatography | | Dissolution 〈711〉 | NLT 75% (Q) of the labeled amount of acetazolamide (C4H6N4O3S2) is dissolved. | Medium: 0.01 N HCl  Volume: 900 mL  Apparatus: 1  Speed: 100 rpm  Time: 60 minutes | | Uniformity of Dosage Units 〈905〉 | Meet the requirements. | None |  |  |  |  | | --- | --- | --- | | **Acetazolamide tablets, BP monograph [36]** | | | | **Test** | **Acceptance criteria** | **Observations** | | Identification A | The infrared spectrum of the residue is concordant with the reference spectrum of acetazolamide. | Infrared spectrometry | | **Test** | **Acceptance criteria** | **Observations** | | Identification b | The paper exhibits a brownish black color. | None | | Identification b | A greenish blue color or precipitate is produced. | None | | Related substances | Any secondary spot in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (2) (1 %). | Thin-layer chromatography | | Assay | 95.0 to 105.0 % of the stated amount of acetazolamide. | Potentiometric titration | | |

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| 1. **REVISION OF PATENTS (BACKGROUND AND RESTRICTIONS)** |
| See patent revision report. |

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| 1. **REFERENCES** (Specify the references throughout the document with numbers between brackets i.e. [1]) |
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| 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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