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| 1. **GENERAL INFORMATION OF THE PRODUCT TO BE DEVELOPED** | |
| Product name: | Vonoprazan Coated Tablet |
| Type of product (OTC, RX, nutraceutical, cosmetic, other?) | RX |
| Brand name / Generic name | Vonoprazan |
| API(s) |  |
| Strength(s) | Vonoprazan 10 mg and Vonoprazan 20 mg |
| Dosage form | Coated Tablet |
| Route of administration | oral |
| Dose(s) | According to physician's prescription |
| Physical characteristics (Color, size, shape, text printed, etc.) |  |
| Type of packaging material | Box packaging (e.g., CAJA X 5 und MM and CAJA X 30 und CIAL) |
| Commercial presentations | VONOPRAZAN 10 mg TAB CAJA X 5 und MM; VONOPRAZAN 20 mg TAB CAJA X 5 und MM; VONOPRAZAN 10 mg TAB CAJA X 30 und CIAL; VONOPRAZAN 20 mg TAB CAJA X 30 und CIAL |
| Expiration time required |  |
| **Observations:** | |

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| 1. **GENERAL INFORMATION OF THE ACTIVE PHARMACEUTICAL INGREDIENT (API) ()** | |
| Common name: | Vonoprazan Fumarate |
| CAS number: | 1260141-27-2 |
| Description: |  |
| Solubility: |  |
| Melting point: | Información no disponible |
| Polymorphs: | Data Analysis: The polymorphic forms of Vonoprazan Fumarate have been rigorously characterized using advanced X‐ray Powder Diffraction and Differential Thermal Analysis methods. Patent CN105315258A reports two distinct crystalline forms, designated as Form A and Form B, prepared via controlled crystallization employing a methyl alcohol-water solvent system at 50–60 °C. Characteristic diffraction peaks observed at 12.253, 13.559, 15.259, 16.889, 17.422, 20.399, 20.764, 22.478, 25.198, and 28.077 degrees confirm unique lattice arrangements. The Differential Thermal Analysis indicates a thermal absorption peak at approximately 209.0 °C, signifying defined thermal behavior and stability. Furthermore, Dr. Reddy’s Laboratories documentation confirms the manufacture of a consistent innovator polymorph that meets in-vivo performance specifications [https://api.drreddys.com/white-paper/product-alert-vonoprazan-fumarate]. Additional compound details are available from PubChem [https://pubchem.ncbi.nlm.nih.gov/compound/Vonoprazan-Fumarate] and corroborated by patents [https://patents.google.com/patent/CN105315258A/en] and [https://patents.google.com/patent/CN105566295A/en]. Control over polymorphism is critical for ensuring dissolution, bioavailability, and overall API efficacy. Rigorous characterization of these solid state properties supports process optimization and regulatory compliance, enhancing product reproducibility and quality assurance for scalable manufacturing processes. Technical Details: The observed polymorphs exhibit distinct crystal habits and lattice energies, offering advantages in dissolution rates and stability, which are pivotal for achieving reliable bioequivalence. Such comprehensive solid state characterization is essential for quality control and optimizing clinical performance overall. |
| Stability (Solid state/solution, general information): |  |
| Scheme of degradation route | Forced degradation studies of Vonoprazan Fumarate API reveal a comprehensive degradation scheme elucidated using robust reversed phase liquid chromatography methods. Analytical data indicate that exposure to varied stress conditions including acidic, alkaline, oxidative, thermal, and photolytic environments facilitates distinct degradation pathways. Under alkaline and oxidative stress, significant API degradation occurred producing multiple degradation products, while stability was preserved during acidic, thermal, and photolytic exposures. The method employed an XSelect CSH Phenyl-Hexyl column with a mobile phase composed of 0.1% trifluoroacetic acid aqueous solution and acetonitrile, with UV detection at 252 nm ensuring clear resolution between the API and its degradants. Additional studies using C18 columns further confirmed the stability-indicating power with characteristic retention times and acceptable peak resolutions. Stability testing, performed in accordance with ICH guidelines, demonstrated that the discharge of degradation products did not interfere with the accurate quantification of active drug content. The degradation scheme thereby supports robust quality assurance and process development measures. The validation of forced degradation studies is essential for assigning safe manufacturing parameters for Vonoprazan Fumarate. Relevant references include [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0026265X24016473), [Egyptian Journal of Chemistry](https://ejchem.journals.ekb.eg/article\_311267\_572167d2524cba3f630a51b4c139db74.pdf), and [PubMed](https://pubmed.ncbi.nlm.nih.gov/29112902/). These forced degradation insights assist regulatory compliance and inform controlled manufacturing conditions for optimal drug performance effectively. |
| Stability indicators |  |
| Impurities (Synthetic origin, degradation products and/or metabolites) | The impurity profile of Vonoprazan Fumarate API is defined by a range of pharmacopeial and non‐pharmacopeial impurities that are critical for quality control and regulatory compliance. Detailed reference standards include compounds such as Vonoprazan Sulfonyl Aldehyde Impurity (CAS: 881677-11-8, molecular formula C16H11FN2O3S, molecular weight 330.33 g/mol) and (5-(2-Fluorophenyl)-1-(pyridin-3-ylsulfonyl)-1H-pyrrol-3-yl)methanol (CAS: 2169271-28-5, molecular weight 332.35 g/mol). The impurity list extends to derivatives such as Vonoprazan Fumarate Impurity 1 (CAS: 2250243-23-1, molecular formula C33H27F2N5O4S2, molecular weight 659.73 g/mol) and deuterated analogues including Vonoprazan Fumarate 13C D3 and Vonoprazan-d4 Fumarate. Structural elucidation is achieved with advanced techniques including mass spectrometry and nuclear magnetic resonance, integrated into stability studies and method validation protocols. Meticulous profiling of these impurities is crucial for ensuring batch-to-batch consistency as well as meeting stringent regulatory standards for ANDA and DMF submissions. Comprehensive analytical data and reference details are available from resources such as [Pharmaffiliates](https://www.pharmaffiliates.com/en/parentapi/vonoprazan-impurities), [Pharmaffiliates Fumarate](https://www.pharmaffiliates.com/en/parentapi/vonoprazan-fumarate-impurities), [ChemicalBook](https://www.chemicalbook.com/ChemicalProductProperty\_EN\_CB63144884.htm), [PubChem](https://pubchem.ncbi.nlm.nih.gov/compound/Vonoprazan-Dimer-Impurity) and [SynZeal](https://www.synzeal.com/en/vonoprazan). |
| Biopharmaceutical classification (Biopharmaceutical classification system) | Vonoprazan Fumarate, the fumarate salt form of a potent potassium‐competitive acid blocker, displays a distinct biopharmaceutical classification that has been documented as BCS Class II/IV. This designation indicates that the drug may exhibit low solubility and/or variable permeability characteristics under differing gastrointestinal pH conditions, factors which are critical in predicting its oral absorption and overall bioavailability. The dual classification suggests that under certain experimental or formulation conditions, intrinsic solubility limitations may be counterbalanced by high membrane permeability, or alternatively, that a complex interplay of solubilization dynamics and drug metabolism could influence the in vivo performance. Such variability necessitates rigorous evaluation using standardized dissolution and permeability protocols to establish a definitive classification. Detailed understanding of this classification is vital for formulation scientists aiming to optimize the dosage form and improve therapeutic consistency. The physicochemical and biopharmaceutical data of Vonoprazan Fumarate, including its molecular properties and salt form, have been corroborated by multiple sources, providing critical insight into its behavior during drug development. Further in vivo and in vitro investigations are recommended to resolve any remaining ambiguities regarding its BCS categorization. Citations: [Bcs Database (K-z)](https://www.pharmaspecialists.com/p/available-bcs-classification-of-drugs-2.html), [PubChem](https://pubchem.ncbi.nlm.nih.gov/compound/Vonoprazan-Fumarate). |
| Toxicological classification (Contention level): |  |
| Other information: | **INN:** Vonoprazan Fumarate  **Chemical names:**  **Structure:**  **Molecular formula:** C21H20FN3O6S  **Molecular mass:** 461.5  **Type of substance:**  **Dissociation constant (pKa):** Información no disponible  **Partition coefficient:** Información no disponible  **Hygroscopicity:** Data Analysis: The hygroscopicity of Vonoprazan Fumarate, an orally active potassium-competitive acid blocker used for acid-related diseases, has been indirectly assessed through its recommended storage and solvent handling requirements. The manufacturer recommends storage at 4°C in sealed containers that are kept away from moisture and light. This storage condition suggests that the API may be sensitive to hygroscopic effects which can compromise its stability by moisture absorption. An additional solvent storage guideline states that in solution, the API must be stored at -80°C for six months or at -20°C for one month, also emphasizing sealed storage, to ensure that moisture-induced degradation is minimized, thereby preserving purity and activity under controlled humidity conditions. The specific details imply that caution is warranted when exposing the API to ambient moisture, which could trigger physical alterations or impurities. The handling measures represent standard best practices for hygroscopic compounds. Detailed citation information is available from the MedChemExpress Datasheet [source](https://file.medchemexpress.com/batch\_PDF/HY-15295/Vonoprazan-Fumarate-DataSheet-MedChemExpress.pdf) and from ChemicalBook [source](https://www.chemicalbook.com/ChemicalProductProperty\_EN\_CB32628441.htm). The controlled storage recommendations highlight the compound’s potential susceptibility to moisture uptake during handling, formulation, and long-term stability studies. Rigorous quality control and environmental monitoring are recommended in pharmaceutical processing. Strict adherence to moisture control is absolutely essential during manufacturing.  **Chirality/Specific optical rotation:** The investigation into the chirality and specific optical rotation of Vonoprazan Fumarate has been informed by general principles of optical activity in chiral compounds. Standard methodologies, such as polarimetric analysis using sodium D line light (589.3 nm) under controlled conditions, are routinely employed to determine the ability of chiral molecules to rotate plane-polarized light. Detailed procedural guidelines and applications have been outlined in literature, notably in discussions of specific rotation in chiral compounds [Science Mania Chemistry](https://www.sciencemaniachem.com/blog/conceptual-blog-for-chemistry-1/understanding-specific-rotation-a-key-property-of-chiral-compounds-1) and pharmacopeial monographs [Digicollections](https://digicollections.net/phint/pdf/b/7.1.4.1.4-Determination-of-optical-rotation-and-specific-ro\_.pdf). Supplementary theoretical treatments and experimental validations are available in academic resources [Chem LibreTexts](https://chem.libretexts.org/Bookshelves/Organic\_Chemistry/Basic\_Principles\_of\_Organic\_Chemistry\_(Roberts\_and\_Caserio)/19:\_More\_on-Stereochemistry/19.02:\_Specific\_Rotation) and recent studies [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0022285218300663) as well as [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S1386142519306791). However, comprehensive, API-specific data including exact numerical values for Vonoprazan Fumarate is not currently available in the provided literature. Further dedicated experimental studies would be required to determine precise values and assess the enantiomeric purity of this API.  **Degradation temperature:**No online available information.  An exhaustive review of the current literature and verified online databases related to Vonoprazan Fumarate did not reveal any explicit measurement or discussion regarding the glass transition temperature of the API. The provided sources predominantly focus on impurity profiling, stability studies, synthesis protocols, and analytical testing methodologies without including any quantifiable data or experimental analysis for the glass transition temperature parameter. Reputable references such as Pharmaffiliates (https://www.pharmaffiliates.com/en/parentapi/vonoprazan-impurities) and ChemicalBook (https://www.chemicalbook.com/ProductChemicalPropertiesCB52716735\_EN.htm) document various physicochemical characteristics like melting point and reaction conditions. Similarly, details from BOC Sciences (https://www.bocsci.com/product/vonoprazan-fumarate-cas-1260141-27-2-457791.html) and Nawah Scientific (https://nawah-scientific.com/all-services/analytical-standards/api/vonoprazan-fumarate/) elaborate on synthesis schemes and metabolic disposition pathways. However, none of these resources provide empirical evidence or studies addressing the glass transition temperature. This notable absence of information underscores the need for further research using techniques such as differential scanning calorimetry to evaluate this critical thermal property. Until such data become available in the scientific literature, the glass transition temperature remains an undetermined parameter in the comprehensive physicochemical profile of Vonoprazan Fumarate.  **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) | |
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| Brand name/Generic name | VOQUEZNA |
| Packaging\_imgs | |
| Manufacturer | PHATHOM PHARMACEUTICALS INC |
| API | Vonoprazan Fumarate (UNII: 4QW3X4AMLB; vonoprazan - UNII:1R5L3J156G) is the active moiety in this product. It is presented as an oral tablet in two dosage strengths, 13.36 mg and 26.72 mg, with corresponding differences in tablet size, color, and imprint codes. |
| Excipients | For the 13.36 mg tablet formulation, the inactive ingredients (with UNII identifiers) are: Mannitol (UNII: 3OWL53L36A); Microcrystalline Cellulose (UNII: OP1R32D61U); Hydroxypropyl Cellulose, Unspecified (UNII: 9XZ8H6N6OH); Fumaric Acid (UNII: 88XHZ13131); Ascorbic acid (UNII: PQ6CK8PD0R); Croscarmellose sodium (UNII: M28OL1HH48); Magnesium Stearate (UNII: 70097M6I30); Hypromellose, unspecified (UNII: 3NXW29V3WO); Polyethylene Glycol 8000 (UNII: Q662QK8M3B); Titanium Dioxide (UNII: 15FIX9V2JP); and Ferric Oxide Yellow (UNII: EX438O2MRT). For the 26.72 mg tablet formulation, the inactive ingredients are: Mannitol (UNII: 3OWL53L36A); Microcrystalline Cellulose (UNII: OP1R32D61U); Hydroxypropyl Cellulose, Unspecified (UNII: 9XZ8H6N6OH); Fumaric Acid (UNII: 88XHZ13131); Ascorbic acid (UNII: PQ6CK8PD0R); Croscarmellose sodium (UNII: M28OL1HH48); Magnesium Stearate (UNII: 70097M6I30); Hypromellose, unspecified (UNII: 3NXW29V3WO); Polyethylene Glycol 8000 (UNII: Q662QK8M3B); Titanium Dioxide (UNII: 15FIX9V2JP); and Ferric Oxide Red (UNII: 1K09F3G675). |
| Strength(s) | Vonoprazan Fumarate is presented as film-coated tablets designed for oral use. Two tablet strengths are available: 10 mg tablets, which are pale yellow, oval, and debossed with 'V10' on one side, and 20 mg tablets, which are pale red, oval, and debossed with 'V20' on one side. |
| Type of packaging material | The vonoprazan fumarate tablets are dispensed in a 30 in 1 bottle format made of plastic (Type 0: Not a Combination Product). Both the 13.36 mg and 26.72 mg strengths are packaged similarly, with marketing initiation on 11/10/2023 under NDA215151. |
| How supplied | VOQUEZNA (vonoprazan) tablets are supplied as follows: 10 mg tablets, pale yellow, oval, film-coated with debossed V10 on one side and plain on the other, in bottles of 30 (NDC 81520-100-30); 20 mg tablets, pale red, oval, film-coated with debossed V20 on one side and plain on the other, in bottles of 30 (NDC 81520-200-30). Store between 20°C and 25°C (68°F and 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature]. |
| Physical characteristics (Color, size, shape, text printed, etc.) | Vonoprazan Fumarate Tablets: The 13.36 mg tablet is pale yellow, oval, 8 mm in size with an imprint code of V10; the 26.72 mg tablet is pale red, oval, 11 mm in size with an imprint code of V20. Both formulations are designed for oral administration. |
| Storage conditions | Store between 20°C and 25°C (68°F and 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature]. |
| Special characteristics of API and excipients (crystalline form used for the RLD, particle size, etc.) | Vonoprazan fumarate, a potassium‐competitive acid blocker, is chemically described as 1 H-pyrrole-3-methanamine, 5-(2-fluorophenyl)-N-methyl-1-(3-pyridinylsulfonyl)-, (2E)-2-butenedioate (1:1) with an empirical formula of C17H16FN3O2S•C4H4O4 and a molecular weight of 461.5. It is presented as white to nearly white crystals or crystalline powder with a melting point of 194.8°C. Solubility characteristics include: soluble in dimethyl sulfoxide; sparingly soluble in N,N-dimethylacetamide; slightly soluble in N,N-dimethylformamide, methanol, and water; very slightly soluble in ethanol (99.5%); and practically insoluble in 2-propanol, acetone, 1-octanol, and acetonitrile. VOQUEZNA tablets are available in 10 mg (equivalent to 13.36 mg of vonoprazan fumarate) and 20 mg (equivalent to 26.72 mg of vonoprazan fumarate) strengths, formulated as film-coated tablets with inactive ingredients including ascorbic acid, croscarmellose sodium, ferric oxides (red in 20 mg tablets and yellow in 10 mg tablets), fumaric acid, hydroxypropyl cellulose, hypromellose, magnesium stearate, mannitol, microcrystalline cellulose, polyethylene glycol 8000, and titanium dioxide. |
| 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** | |
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| 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]) |
| **[1]** National Center for Biotechnology Information (2022). PubChem Compound Summary for CID 16078, Dronabinol. Retrieved January 4, 2022, from <https://pubchem.ncbi.nlm.nih.gov/compound/Dronabinol>.  **[2]** Dronabinol in Sesame Oil, Product Technical Package, US DMF # 20682, PurisysTM.  **[3]** Ronak Savla, Jeff Browne, Vincent Plassat, Kishor M. Wasan & Ellen K. Wasan (2017) Review and analysis of FDA approved drugs using lipid-based formulations, Drug Development and Industrial Pharmacy, 43:11, 1743-1758.  **[4]** National Center for Biotechnology Information (2022). PubChem Compound Summary for CID 1986, Acetazolamide. Retrieved January 5, 2022, from <https://pubchem.ncbi.nlm.nih.gov/compound/Acetazolamide>.  **[5]** Reference tables: USP. Description and Relative Solubility of USP and NF Articles. In USP-NF. Rockville, MD: USP; January 5, 2022.  **[6]** ChemSpider (2022).Chemical Structure Search, Acetazolamide. 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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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