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| 1. **GENERAL INFORMATION OF THE PRODUCT TO BE DEVELOPED** | |
| Product name: | VONOPRAZAN 10 mg TAB, VONOPRAZAN 20 mg TAB |
| Type of product (OTC, RX, nutraceutical, cosmetic, other?) | RX |
| Brand name / Generic name | Vonoprazan |
| API(s) |  |
| Strength(s) | Vonoprazan 10 mg, Vonoprazan 20 mg |
| Dosage form | Tablet |
| Route of administration | Oral |
| Dose(s) | According to physician's prescription |
| Physical characteristics (Color, size, shape, text printed, etc.) |  |
| Type of packaging material |  |
| 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: | The polymorphic forms of Vonoprazan Fumarate API have been characterized by distinct crystalline profiles that are critical for ensuring consistent pharmacokinetic and manufacturing performance. Detailed studies using X‐ray Powder Diffraction with Cu-Kα radiation have identified several characteristic 2θ diffraction peaks at 12.253°, 13.559°, 15.259°, 16.889°, 17.422°, 20.399°, 20.764°, 22.478°, 25.198°, and 28.077°. These peaks serve as unique fingerprints to distinguish at least two crystalline forms, designated as Form A and Form B, a finding further corroborated by Differential Thermal Analysis which exhibits a prominent absorption peak at approximately 209.0°C. The existence of multiple polymorphs may influence solubility, stability, and bioavailability profiles, hence a rigorous screening and control process is essential during API manufacturing. Patent CN105315258A outlines a robust method to obtain these crystalline forms with a molar yield of 79.8%, underscoring the feasibility of industrial scale-up. Furthermore, product data provided by Dr. Reddy’s Laboratories confirms adherence to cGMP standards by consistently supplying the innovator crystalline form, ensuring reproducibility and quality in the final drug product. These analytical results, as reported in detail by the patent and confirmed by drug manufacturer profiles, are integral to the comprehensive understanding and regulatory acceptance of the API [PubChem](https://pubchem.ncbi.nlm.nih.gov/compound/Vonoprazan-Fumarate) [CN105315258A](https://patents.google.com/patent/CN105315258A/en) [Dr. Reddy’s Laboratories](https://api.drreddys.com/white-paper/product-alert-vonoprazan-fumarate). |
| Stability (Solid state/solution, general information): |  |
| Scheme of degradation route | Vonoprazan fumarate, a potent potassium‐competitive acid blocker, has been rigorously evaluated through forced degradation studies to elucidate its degradation pathways under diverse stress conditions. An optimized reversed‐phase liquid chromatography method, utilizing a CSH Phenyl‐Hexyl column with a stepped gradient of 0.1% trifluoroacetic acid aqueous solution and acetonitrile at 25 °C, was employed to monitor degradation [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0026265X24016473). The degradation protocol encompassed acidic, alkaline, oxidative, thermal, and photolytic conditions, providing a comprehensive view of VPZ’s chemical stability. Significant degradation was observed under alkaline and oxidative stress, which facilitated detection and quantification of specific degradants without interference in the VPZ assay [PubMed](https://pubmed.ncbi.nlm.nih.gov/29112902/). Further, method validation incorporating response surface methodology and tolerance analysis confirmed six sigma quality performance. Supplementary evaluations demonstrated that the degradation products, identified via stability-indicating HPLC, followed predictable pathways that are critical for process development and quality assurance [Eurekamag](https://eurekamag.com/research/059/598/059598982.php). Corroborative investigations using complementary techniques further detailed the degradation scheme and offered robust support for the analytical findings [ResearchGate](https://www.researchgate.net/publication/320958087\_Development\_of\_a\_stability-\_indicating\_HPLC\_method\_for\_simultaneous\_determination\_of\_ten\_related\_substances\_in\_vonoprazan\_fumarate\_drug\_substance). |
| Stability indicators |  |
| Impurities (Synthetic origin, degradation products and/or metabolites) | An extensive impurity profile has been established for the Vonoprazan Fumarate API using advanced analytical techniques such as high-performance liquid chromatography, mass spectrometry, and nuclear magnetic resonance. Comprehensive assessment of impurities is critical for ensuring the purity, potency, and safety of the drug substance. Multiple impurities including pharmacopeial and non-pharmacopeial byproducts have been identified and characterized. For instance, Vonoprazan Sulfonyl Aldehyde Impurity (CAS 881677-11-8, molecular weight 330.33 g/mol) is among the key impurities, while others display molecular weights ranging from approximately 204 to 688 g/mol. Predictive studies report that certain impurities, such as the Vonoprazan Fumarate impurity with CAS 1885094-62-1 (molecular weight 359.42 g/mol), exhibit a boiling point around 514.2 ± 60.0 °C and a density near 1.26 ± 0.1 g/cm3. These impurities, whether arising from synthetic routes, degradation processes or storage conditions, are rigorously monitored to maintain regulatory compliance. Data from multiple sources confirm the impurity profiles and support method validation for impurity quantification [Pharmaffiliates](https://www.pharmaffiliates.com/en/parentapi/vonoprazan-fumarate-impurities), [ChemicalBook](https://www.chemicalbook.com/ChemicalProductProperty\_EN\_CB63144884.htm), and [Clearsynth](https://www.clearsynth.com/product-category/Impurities/Vonoprazan-Impurities). Stringent impurity characterization protocols and validated testing methods ensure that impurities are identified quantitatively, contributing to robust quality control and compliance with international regulatory standards, thereby safeguarding patient safety effectively. |
| Biopharmaceutical classification (Biopharmaceutical classification system) | Vonoprazan Fumarate, a potent reversible potassium‐competitive acid blocker, has been evaluated under the Biopharmaceutics Classification System (BCS) framework to support biowaiver applications and optimize oral dosage design. The BCS integrates solubility, permeability, and dissolution rate to predict in vivo drug absorption. Although specific numerical values for these parameters are not detailed in the provided sources, available literature suggests that Vonoprazan Fumarate exhibits physicochemical properties conducive to high solubility and favorable dissolution, meeting essential ICH M9 criteria [https://www.criver.com/products-services/lab-sciences/bcs-classification-biowaivers]. The comprehensive PubChem profile [https://pubchem.ncbi.nlm.nih.gov/compound/Vonoprazan-Fumarate] furnishes foundational data supporting further experimental assessment. Additionally, the online BCS Classification Database at Pharmaspecialists [https://www.pharmaspecialists.com/2021/08/online-bcs-classification-database.html] highlights the role of BCS data for streamlining regulatory submissions by potentially waiving in vivo bioequivalence studies. Rigorous in vitro dissolution and permeability experiments are recommended to definitively assign the API to a BCS category. Further experimental validation through standardized in vitro assays is essential to confirm release kinetics and intestinal permeability characteristics. Such data will provide regulatory confidence and facilitate streamlined entry. |
| 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:** A review of available data for Vonoprazan Fumarate reveals no explicit quantitative hygroscopicity values despite detailed storage recommendations provided in multiple sources. The product datasheets from MedChemExpress and SelleckChem specify storage conditions of 4°C in sealed containers and advise that the material be kept away from moisture and light, indicating a precautionary stance toward potential moisture sensitivity. In solvent systems, storage under reduced temperatures (–80°C or –20°C) in sealed conditions is advised to maintain stability. These recommendations imply that inadvertent moisture exposure could negatively impact the API’s performance; however, no numerical metrics such as moisture uptake percentages or dynamic vapor sorption data have been disclosed. PubChem profiles similarly lack detailed hygroscopicity measurements for this compound. In sum, while the controlled storage conditions suggest that Vonoprazan Fumarate may exhibit hygroscopic behavior, the available evidence does not include direct experimental quantification of moisture absorption. Researchers are therefore urged to adhere strictly to the manufacturer’s guidelines to mitigate any potential degradation due to moisture. [MedChemExpress](https://file.medchemexpress.com/batch\_PDF/HY-15295/Vonoprazan-Fumarate-DataSheet-MedChemExpress.pdf) [SelleckChem](https://www.selleckchem.com/datasheet/vonoprazan-fumarate-E498801-DataSheet.html) [PubChem](https://pubchem.ncbi.nlm.nih.gov/compound/Vonoprazan-Fumarate)  **Chirality/Specific optical rotation:** No online available information.  **Degradation temperature:**An extensive review of available online sources reveals that no explicit degradation temperature has been reported for Vonoprazan Fumarate API. While detailed information on physical properties, impurity profiles, and forced degradation studies is available, none of the sources clearly state a specific temperature at which the API degrades. For instance, the Pharmaffiliates portal (https://www.pharmaffiliates.com/en/parentapi/vonoprazan-fumarate-impurities) provides comprehensive data on impurities and analytical methods without offering numerical degradation temperature values. Similarly, the datasheets available from SelleckChem (https://www.selleckchem.com/datasheet/vonoprazan-fumarate-E498801-DataSheet.html) and ChemicalBook (https://www.chemicalbook.com/ProductChemicalPropertiesCB52716735\_EN.htm) document melting point information and other physicochemical characteristics, yet they do not specify a degradation temperature. Although forced degradation studies have been referenced in the literature, any associated thermal degradation parameters remain unspecified. As such, further analyses employing thermal techniques such as differential scanning calorimetry would be necessary to determine this parameter. In summary, the current publicly available evidence does not include degradation temperature data for Vonoprazan Fumarate API, and therefore no definitive value can be reported at this time.  No online available information regarding the glass transition temperature of Vonoprazan Fumarate API was identified from the provided sources. The available evidence primarily details other physicochemical parameters such as melting point, molecular weight, and solubility details, but does not provide any data on the amorphous-to-glassy state transition characteristics typically measured by techniques such as differential scanning calorimetry (DSC) or dynamic mechanical analysis (DMA). In the current dataset, references including the LGC Standards webpage [LGC Standards](https://www.lgcstandards.com/AZ/en/Vonoprazan-Fumarate/p/MM3871.01-0250) and the MedChemExpress data sheet [MedChemExpress](https://file.medchemexpress.com/batch\_PDF/HY-15295/Vonoprazan-Fumarate-DataSheet-MedChemExpress.pdf) focus instead on impurity profiling, melting point (approximately 194.8°C), and storage conditions. Similarly, ChemicalBook sources [ChemicalBook](https://www.chemicalbook.com/ChemicalProductProperty\_EN\_CB52716735.htm) provide extensive chemical properties but omit any mention of glass transition temperature. As a result, no validated experimental or analytical measurements for the glass transition temperature of Vonoprazan Fumarate API are currently available in the examined literature.  **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 presented in two oral tablet formulations with strengths of 13.36 mg and 26.72 mg. Both formulations feature similar inactive ingredients and are manufactured as oval tablets, with the 13.36 mg tablet exhibiting a pale yellow color and an 8 mm size, and the 26.72 mg tablet demonstrating a pale red hue and an 11 mm size. Packaging details include a 30 in 1 bottle configuration, marketed under NDA215151 by Phathom Pharmaceuticals Inc. |
| Excipients | For the vonoprazan fumarate tablet, two strengths are provided. For the 13.36 mg strength, the inactive ingredients include: 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 strength, the inactive ingredients include: 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) | The product is supplied as tablets in two dosage strengths: • 10 mg of vonoprazan: pale yellow, oval, film-coated tablets debossed V10 on one side and plain on the other side; • 20 mg of vonoprazan: pale red, oval, film-coated tablets debossed V20 on one side and plain on the other side. |
| Type of packaging material | Vonoprazan fumarate tablets are available in two strengths with distinct packaging characteristics. The 13.36 mg formulation, with a pale yellow color, oval shape (8 mm) and imprint code V10, is supplied in a plastic bottle containing 30 units. The 26.72 mg formulation, featuring a pale red color, oval shape (11 mm) and imprint code V20, is similarly provided in a plastic 30-count bottle (Type 0: Not a Combination Product) with a marketing start date of 11/10/2023. |
| How supplied | VOQUEZNA (vonoprazan) tablets are supplied in two strengths. The 10 mg tablets are pale yellow, oval, film-coated with a debossed 'V10' on one side and plain on the other, packaged in bottles of 30 (NDC 81520-100-30). The 20 mg tablets are pale red, oval, film-coated with a debossed 'V20' on one side and plain on the other, packaged in bottles of 30 (NDC 81520-200-30). Storage conditions are between 20°C and 25°C (68°F and 77°F) with permitted excursions between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature]. |
| Physical characteristics (Color, size, shape, text printed, etc.) | VOQUEZNA vonoprazan fumarate tablets are provided in two strengths. The 13.36 mg tablet is characterized by a pale yellow color, an oval shape, an 8 mm size, and an imprint code of V10. The 26.72 mg tablet exhibits a pale red color, an oval shape, an 11 mm size, and an imprint code of V20. |
| 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, the fumarate salt of vonoprazan, is a potassium‐competitive acid blocker with an empirical formula of C17H16FN3O2S•C4H4O4 and a molecular weight of 461.5. It appears as white to nearly white crystals or crystalline powder with a melting point of 194.8°C. The compound is 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 and 20 mg strengths (equivalent to 13.36 mg and 26.72 mg of vonoprazan fumarate, respectively) and include inactive ingredients such as ascorbic acid, croscarmellose sodium, ferric oxide red or yellow (depending on the dosage), 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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