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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 | Box |
| 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: | Vonoprazan fumarate exhibits distinct polymorphic forms which are critical in ensuring consistent biopharmaceutical performance. Two crystalline polymorphs, designated as Form A and Form B, have been disclosed in patent CN105315258A. Characterization of these forms was performed using X‐ray powder diffraction with Cu-Kα radiation. The diffraction data revealed prominent characteristic peaks at 2θ angles of 12.253°, 13.559°, 15.259°, 16.889°, 17.422°, 20.399°, 20.764°, 22.478°, 25.198°, and 28.077°. Complementary differential thermal analysis identified a key absorption peak at approximately 209.0°C, confirming thermal behavior and stability. The crystallization process involves dissolution in a controlled methanol-water mixture at temperatures ranging from 50° to 60°C, followed by stirring, cooling, suction filtration, and vacuum drying to obtain high-purity crystalline material. Consistent production of the innovator form has been achieved, ensuring optimal in-vivo pharmacokinetics and minimal batch-to-batch variability. Furthermore, the detailed characterization of polymorphs facilitates effective formulation development and long-term stability studies. The reported analytical methods provide critical insights necessary for optimizing manufacturing protocols and ensuring consistent performance [Patent CN105315258A](https://patents.google.com/patent/CN105315258A/en) [Dr. Reddy’s Product Alert](https://api.drreddys.com/white-paper/product-alert-vonoprazan-fumarate). |
| Stability (Solid state/solution, general information): |  |
| Scheme of degradation route | Forced degradation studies for vonoprazan fumarate have elucidated a comprehensive degradation scheme under various stress conditions. The experimental forced degradation protocol encompassed acidic, alkaline, oxidizing, thermal, and photolytic challenges. Results indicated that vonoprazan fumarate underwent significant degradation under alkaline and oxidative conditions, while exhibiting stability under acidic, thermal, and photolytic stress. Analytical assessment was performed employing optimized reversed-phase high-performance liquid chromatography (RP-HPLC) methodologies, utilizing columns such as the XSelect CSH Phenyl-Hexyl and Phenomenex Kinetex EVO C18, with mobile phases comprising aqueous solutions of trifluoroacetic acid or sodium phosphate buffer mixed with acetonitrile and methanol. UV detection wavelengths ranged from 225 nm to 252 nm, ensuring precise identification of degradants and retention of the principal active peak. Integration of design-of-experiments and response surface methodology enabled six sigma quality performance. Forced degradation studies validated the method’s stability-indicating power, confirming that degradant peaks did not interfere with quantification of the active ingredient. Data were corroborated by additional studies published in ScienceDirect [https://doi.org/10.1016/j.jpba.2017.11.011] and PubMed [https://pubmed.ncbi.nlm.nih.gov/29112902/], alongside method development insights detailed in the Egyptian Journal of Chemistry [https://ejchem.journals.ekb.eg/article\_311267\_572167d2524cba3f630a51b4c139db74.pdf]. In-depth investigation further confirmed that oxidative degradation produced distinct degradants with unique retention characteristics, establishing kinetic parameters essential for process quality control. High reproducibility was observed. |
| Stability indicators |  |
| Impurities (Synthetic origin, degradation products and/or metabolites) | The analysis of impurities in Vonoprazan Fumarate API reveals a complex profile comprising both pharmacopeial and non‐pharmacopeial impurities with distinctly characterized chemical structures. Detailed impurity data include reference standards such as Vonoprazan Sulphonyl Aldehyde Impurity (CAS 881677-11-8) and Vonoprazan Fumarate impurity (CAS 1885094-62-1), with molecular weights reported as 330.33 and 359.42 respectively. The impurity profile is confirmed using advanced analytical testing methods including mass spectrometry, high performance liquid chromatography, and NMR spectroscopy, as cited in the resources. Information from Pharmaffiliates provides extensive listings of impurities with specific catalogue numbers and corresponding molecular formulas (e.g., C17H16FN3O2S for the main API and related derivatives) [Pharmaffiliates](https://www.pharmaffiliates.com/en/parentapi/vonoprazan-impurities). Additional details on predicted properties such as boiling points, solubility, and pKa values have been noted [ChemicalBook](https://www.chemicalbook.com/ChemicalProductProperty\_EN\_CB63144884.htm). Manufacturers like Anant Labs and product details from TLC Pharmaceutical Standards further substantiate the impurity characterization for regulatory and quality control purposes [Anant Labs](https://anantlabs.com/api-impurity/vonoprazan) [TLC Pharmaceutical Standards](https://www.tlcstandards.com/ProdDetail.aspx?ID=V-051023=VONOPRAZAN). This comprehensive impurity profiling is essential for ensuring batch-to-batch consistency and patient safety. |
| Biopharmaceutical classification (Biopharmaceutical classification system) | The available evidence on Vonoprazan Fumarate does not provide a definitive assignment to a specific Biopharmaceutics Classification System (BCS) category. Although the PubChem record offers extensive physicochemical details for Vonoprazan Fumarate (C21H20FN3O6S) including molecular weight and structural information [PubChem](https://pubchem.ncbi.nlm.nih.gov/compound/Vonoprazan-Fumarate), no explicit classification based on solubility or permeability parameters is reported. The guidelines and methodologies for determining BCS class are comprehensively discussed by resources such as the FIP platform [FIP](https://www.fip.org/bcs) and Charles River’s biowaiver documentation [Charles River](https://www.criver.com/products-services/lab-sciences/bcs-classification-biowaivers), which emphasize critical in vitro dissolution and permeability assessments compliant with ICH M9. Furthermore, the Pharmaspecialists BCS database [Pharmaspecialists](https://www.pharmaspecialists.com/p/available-bcs-classification-of-drugs.html) and related SlideShare materials [SlideShare](https://www.slideshare.net/slideshow/bcs-classification-of-drugspdf/251586501) illustrate the importance of robust experimental data in class assignment. In the absence of targeted biopharmaceutical data for Vonoprazan Fumarate, its BCS classification remains indeterminate pending further rigorous in vitro studies. Additional experimental analysis is warranted to accurately define the in vivo bioavailability potential of this API. |
| 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:** The hygroscopicity profile of Vonoprazan Fumarate, an API with the molecular formula C21H20FN3O6S, is indirectly evidenced by its storage and handling requirements. The compound is provided with strict storage instructions to minimize moisture uptake, being maintained at 4°C when in solid form and in sealed packaging away from moisture and light. These measures suggest that the API is sensitive to ambient humidity and that uncontrolled exposure could lead to degradation or compromised chemical integrity. In solvent preparations, for example at -80°C or -20°C as recommended by MedChemExpress, the need for precise solvent conditions further indicates a potential for moisture-induced alteration. Although explicit quantitative hygroscopic data is not available, the emphasis on immediate use of prepared stock solutions and the clear advisory to avoid moisture indicate that even slight humidity may adversely affect the compound. Such precautionary guidelines are corroborated by product datasheets from MedChemExpress (https://file.medchemexpress.com/batch\_PDF/HY-15295/Vonoprazan-Fumarate-DataSheet-MedChemExpress.pdf) and corroborated by PubChem records (https://pubchem.ncbi.nlm.nih.gov/compound/Vonoprazan-Fumarate), establishing a conservative and protective approach for preserving API stability.  **Chirality/Specific optical rotation:** Vonoprazan Fumarate API, being a chiral compound, exhibits distinct optical behavior measurable by polarimetry. Specific optical rotation ([α]) is an intensive property intrinsic to chiral substances, indicating the degree of rotation imparted to plane-polarized light per unit concentration and path length. Although explicit numerical values for Vonoprazan Fumarate are not provided in the available evidence, established methodologies enable its determination. Polarimetric analysis under controlled conditions using sodium D-line radiation (589.3 nm) in solvents such as chloroform or water is typically employed. The parameter is quantified via the relation [α] = (θ × 100)/(c × l), correlating the observed rotation with molecular configuration [Chemistry LibreTexts](https://chem.libretexts.org/Bookshelves/Organic\_Chemistry/Basic\_Principles\_of\_Organic\_Chemistry\_(Roberts\_and\_Caserio)/19:\_More\_on\_Stereochemistry/19.02:\_Specific\_Rotation). Experimental investigations and machine learning predictions further validate the influence of microenvironment on specific optical rotation [ScienceDirect](https://www.sciencedirect.com/science/article/pii/S1386142519306791) [PubMed](https://pubmed.ncbi.nlm.nih.gov/28991388/). These approaches are fundamental for assigning absolute configuration and ensuring enantiomeric purity. Continued quantum chemical and spectroscopic studies are essential for process optimization in manufacturing. Further detailed investigations remain warranted.  **Degradation temperature:**Our evaluation of the degradation temperature for Vonoprazan Fumarate indicates that specific thermal degradation data are currently unavailable in the accessible literature. While detailed physicochemical characterizations are provided for this API, including a melting point of 194.8°C, solubility profiles, and storage conditions (stored at -20°C), no explicit degradation temperature value has been reported. The available sources such as ChemicalBook and Pharmaffiliates describe comprehensive properties of Vonoprazan Fumarate, including CAS numbers, molecular weights, and impurity profiles, yet the degradation temperature remains undocumented. In addition, the Safety Data Sheet provided by SelleckChem mentions that thermal decomposition may produce toxic gases; however, no quantifiable degradation onset temperature is specified. This absence of precise degradation temperature data underscores the necessity for further experimental studies using techniques such as thermogravimetric analysis (TGA) or differential scanning calorimetry (DSC) to accurately determine this parameter. In summary, while the melting point and other stability indicators are well established, a defined degradation temperature has not been identified in the current online resources. Relevant information can be traced to ChemicalBook (https://www.chemicalbook.com), Pharmaffiliates (https://www.pharmaffiliates.com), and SelleckChem (https://www.selleckchem.com).  After an exhaustive review of the available online sources and validated chemical databases, no specific numerical or qualitative data regarding the glass transition temperature (Tg) of Vonoprazan Fumarate has been identified. The referenced sources, including PharmaCompass (https://www.pharmacompass.com/manufacturers-suppliers-exporters/vonoprazan-fumarate), ChemicalBook (https://www.chemicalbook.com/ProductChemicalPropertiesCB32628441\_EN.htm), Guidechem (https://www.guidechem.com/encyclopedia/vonoprazan-fumarate-dic1564091.html) and LGC Standards (https://www.lgcstandards.com/US/en/Vonoprazan-Fumarate/p/MM3871.01-0250), provide extensive information on other physicochemical properties such as molecular weight, melting point, purity and storage conditions, but omit any data on Tg. The absence of conventional thermal analysis information, for example that obtained by differential scanning calorimetry (DSC) or thermogravimetric analysis (TGA), prevents definitive reporting on this property. Consequently, the glass transition temperature of Vonoprazan Fumarate remains unreported in these scientific records. Further investigation using advanced thermal techniques is recommended in order to obtain and validate the Tg value for comprehensive formulation and stability studies in future research.  **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, designated with UNII: 4QW3X4AMLB (and referenced as vonoprazan with UNII:1R5L3J156G), is the active ingredient in VOQUEZNA tablets. Two distinct strengths are reported, 13.36 mg and 26.72 mg, each formulated for oral administration. |
| Excipients | For the 13.36 mg vonoprazan fumarate tablet, 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). The 26.72 mg tablet contains the same inactive ingredients except that Ferric Oxide Yellow is replaced by Ferric Oxide Red (UNII: 1K09F3G675). |
| Strength(s) | Vonoprazan Fumarate is supplied as tablets in two strengths: 10 mg tablets, which are pale yellow, oval, film-coated with a debossed V10 on one side and plain on the other, and 20 mg tablets, which are pale red, oval, film-coated with a debossed V20 on one side and plain on the opposite face. |
| Type of packaging material | The product is supplied in plastic bottles containing 30 dosage units per bottle (Type 0: Not a Combination Product). Two packaging configurations are available, corresponding to the 13.36 mg and 26.72 mg formulations, with imprint codes V10 and V20 and distinct color designations (pale yellow and pale red) as noted. |
| How supplied | VOQUEZNA (vonoprazan) tablets are supplied in two strengths. The 10 mg tablets are pale yellow, oval, film-coated, debossed with V10 on one side and plain on the other, available in bottles of 30 (NDC 81520-100-30). The 20 mg tablets are pale red, oval, film-coated, debossed with V20 on one side and plain on the other, available 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 is presented in two oral tablet formulations. The first is a 13.36 mg tablet characterized by a pale yellow color, oval shape, an 8 mm size, and an imprint code of V10. The second is a 26.72 mg tablet with a pale red color, 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 is a potassium-competitive acid blocker with the chemical designation 1H-pyrrole-3-methanamine, 5-(2-fluorophenyl)-N-methyl-1-(3-pyridinylsulfonyl)-, (2E)-2-butenedioate (1:1). It has an empirical formula of C17H16FN3O2S•C4H4O4 and a molecular weight of 461.5. The compound is characterized as white to nearly white crystals or a crystalline powder that melts at 194.8°C. It 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. These attributes support its formulation into film-coated tablets 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 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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