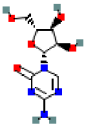
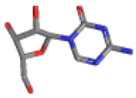
PubChem

COMPOUND SUMMARY

# Azacitidine

| | |
|---|---|
| **PubChem CID** | 9444 |
| **Structure** |  2D  3D<br>Find Similar Structures |
| **Chemical Safety** |  Irritant Health Hazard<br>Laboratory Chemical Safety Summary (LCSS) Datasheet |
| **Molecular Formula** | $C_8H_{12}N_4O_5$ |
| **Synonyms** | 5-azacytidine<br>Azacitidine<br>320-67-2<br>Ladakamycin<br>Azacytidine<br>More... |
| **Molecular Weight** | 244.20 |
| **Dates** | Modify 2022-08-05 Create 2004-09-16 |

Azacitidine is a cytosine analogue and antineoplastic agent used in the therapy of myelodysplastic syndromes. Azacitidine is associated with a low rate of transient serum enzyme elevations during therapy and has only rarely been implicated in cases of clinically apparent acute liver injury with jaundice.

▸ LiverTox

Azacitidine is a pyrimidine nucleoside analogue of cytidine with antineoplastic activity. Azacitidine is incorporated into DNA, where it reversibly inhibits DNA methyltransferase, thereby blocking DNA methylation. Hypomethylation of DNA by azacitidine may activate tumor suppressor genes silenced by hypermethylation, resulting in an antitumor effect. This agent is also incorporated into RNA, thereby disrupting normal RNA function and impairing tRNA cytosine-5-methyltransferase activity. (NCI04)

▸ NCI Thesaurus (NCIt)

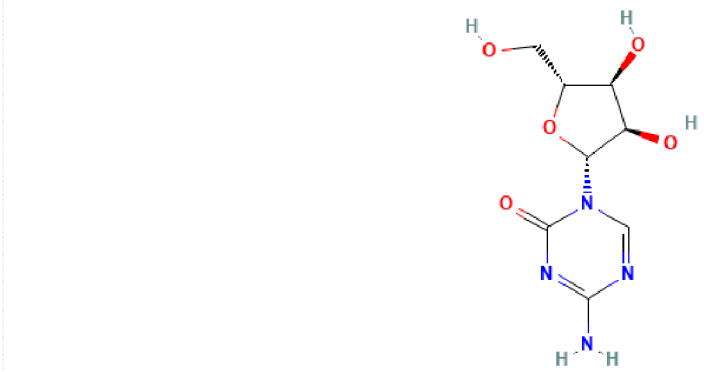
Azacitidine is a Nucleoside Metabolic Inhibitor. The mechanism of action of azacitidine is as a Nucleic Acid Synthesis Inhibitor.

▸ FDA Pharm Classes

# 1 Structures

## 1.1 2D Structure

Chemical Structure Depiction



PubChem

## 1.2 3D Conformer

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## 2 Biologic Description

| | |
|---|---|
| **IUPAC Condensed** | z5Cyt-Ribf |
| **Sequence** | N |
| **HELM** | RNA1{R([*n1cnc(nc1=O)N \|$_R1;;;;;;;$\|])}$$$$ |
| **IUPAC** | 5-aza-cytidine |

PubChem

# 3 Names and Identifiers

## 3.1 Computed Descriptors

### 3.1.1 IUPAC Name

4-amino-1-[(2*R*,3*R*,4*S*,5*R*)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,3,5-triazin-2-one

*Computed by Lexichem TK 2.7.0 (PubChem release 2021.05.07)*

PubChem

### 3.1.2 InChI

InChI=1S/C8H12N4O5/c9-7-10-2-12(8(16)11-7)6-5(15)4(14)3(1-13)17-6/h2-6,13-15H,1H2,(H2,9,11,16)/t3-,4-,5-,6-/m1/s1

*Computed by InChI 1.0.6 (PubChem release 2021.05.07)*

PubChem

### 3.1.3 InChIKey

NMUSYJAQQFHJEW-KVTDHHQDSA-N

*Computed by InChI 1.0.6 (PubChem release 2021.05.07)*

PubChem

### 3.1.4 Canonical SMILES

C1=NC(=NC(=O)N1C2C(C(C(O2)CO)O)O)N

*Computed by OEChem 2.3.0 (PubChem release 2021.05.07)*

PubChem

### 3.1.5 Isomeric SMILES

C1=NC(=NC(=O)N1[C@H]2[C@@H]([C@@H]([C@H](O2)CO)O)O)N

*Computed by OEChem 2.3.0 (PubChem release 2021.05.07)*

PubChem

## 3.2 Molecular Formula

C8H12N4O5

CAMEO Chemicals; PubChem

## 3.3 Other Identifiers

### 3.3.1 CAS

320-67-2

CAMEO Chemicals; CAS Common Chemistry; ChemIDplus; DrugBank; DTP/NCI; EPA DSSTox; European Chemicals Agency (ECHA); Hazardous Substances Data Bank (HSDB); Human Metabolome Database (HMDB)

### 3.3.2 European Community (EC) Number

206-280-2

European Chemicals Agency (ECHA)

### 3.3.3 NSC Number

758186

DTP/NCI

### 3.3.4 UNII

M801H13NRU

FDA/SPL Indexing Data

### 3.3.5 DSSTox Substance ID

DTXSID9020116

EPA DSSTox

### 3.3.6 Wikidata

Q416451

Wikidata

### 3.3.7 NCI Thesaurus Code

C288

NCI Thesaurus (NCIt)

### 3.3.8 RXCUI

1251

NLM RxNorm Terminology

## 3.4 Synonyms

### 3.4.1 MeSH Entry Terms

5 Azacytidine
5-Azacytidine
Azacitidine
Azacytidine
NSC 102816
NSC-102816
NSC102816
Vidaza

Medical Subject Headings (MeSH)

### 3.4.2 Depositor-Supplied Synonyms

| | | | |
|---|---|---|---|
| 5-azacytidine | Azacitidina [INN-Spanish] | M801H13NRU | U-18,496 |
| Azacitidine | NSC-102816 | 4-amino-1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-1,3,5-triazin-2(1H)-one | CCRIS 60 |
| 320-67-2 | C8H12N4O5 | 4-Amino-1-(beta-D-ribofuranosyl)-1,3,5-triazin-2(1H)-one | SMR0008572 |
| Ladakamycin | NSC 102816 | MFCD00006539 | Vidaza (TN) |
| Azacytidine | U-18496 | 4-amino-1-[(2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,3,5-triazin-2-one | HSDB 6879 |
| Vidaza | 4-Amino-1-beta-D-ribofuranosyl-s-triazin-2(1H)-one | 4-amino-1-[(2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,2-dihydro-1,3,5-triazin-2-one | 5-aza-CR |
| Mylosar | UNII-M801H13NRU | WR-183027 | SR-01000075 |
| 5-azacitidine | NSC102816 | NCGC00090851-04 | EINECS 206-2 |
| Azacitidinum | 5AzaC | DSSTox_CID_116 | BRN 062046 |
| Azacitidina | 4-Amino-1-beta-d-ribofuranosyl-1,3,5-triazin-2(1H)-one | U 18496 | Onureg |
| Azacitidinum [INN-Latin] | Antibiotic U 18496 | DSSTox_RID_75378 | Azacitidine (J |
| 5-AZAC | CHEBI:2038 | DSSTox_GSID_20116 | Azacitidine [I |

PubChem

# 4 Chemical and Physical Properties

## 4.1 Computed Properties

| Property Name | Property Value | Reference |
|---|---|---|
| Molecular Weight | 244.20 | Computed by PubChem 2.1 (PubChem release 2021.05.07) |
| XLogP3 | -2.2 | Computed by XLogP3 3.0 (PubChem release 2021.05.07) |
| Hydrogen Bond Donor Count | 4 | Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07) |
| Hydrogen Bond Acceptor Count | 5 | Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07) |
| Rotatable Bond Count | 2 | Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07) |
| Exact Mass | 244.08076950 | Computed by PubChem 2.1 (PubChem release 2021.05.07) |
| Monoisotopic Mass | 244.08076950 | Computed by PubChem 2.1 (PubChem release 2021.05.07) |
| Topological Polar Surface Area | 141 Å² | Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07) |
| Heavy Atom Count | 17 | Computed by PubChem |
| Formal Charge | 0 | Computed by PubChem |
| Complexity | 384 | Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07) |
| Isotope Atom Count | 0 | Computed by PubChem |
| Defined Atom Stereocenter Count | 4 | Computed by PubChem |
| Undefined Atom Stereocenter Count | 0 | Computed by PubChem |
| Defined Bond Stereocenter Count | 0 | Computed by PubChem |
| Undefined Bond Stereocenter Count | 0 | Computed by PubChem |
| Covalently-Bonded Unit Count | 1 | Computed by PubChem |
| Compound Is Canonicalized | Yes | Computed by PubChem (release 2021.05.07) |

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## 4.2 Experimental Properties

### 4.2.1 Physical Description

5-azacytidine is a white crystalline powder. (NTP, 1992)

*National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.*

CAMEO Chemicals

Solid

Human Metabolome Database (HMDB)

### 4.2.2 Color/Form

Crystals from methanol

*Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 153*

Hazardous Substances Data Bank (HSDB)

### 4.2.3 Melting Point

442 to 446 °F (decomposes) (NTP, 1992)

*National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.*

CAMEO Chemicals

229 °C

*PhysProp*

DrugBank

229.0 °C

EPA DSSTox

228-230 °C (decomposes)

*Aldrich; Aldrich Handbook of Fine Chemicals and Laboratory Equipment. 2000-2001. Milwaukee, WI: Aldrich Chem Co. p. 132 (2000)*

Hazardous Substances Data Bank (HSDB)

229°C

Human Metabolome Database (HMDB)

### 4.2.4 Solubility

>36.6 [ug/mL]

- Burnham Center for Chemical Genomics

5 to 10 mg/mL at 70° F (NTP, 1992)

*National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.*

- CAMEO Chemicals

89000 mg/L

- DrugBank

1.21e+01 g/L

- Human Metabolome Database (HMDB)

DMSO 52.7 (mg/mL)

- NCI Investigational Drugs

Distilled H2O 13.7-14.0 (mg/mL)

- NCI Investigational Drugs

0.1 N HCL 27.7-28.0 (mg/mL)

- NCI Investigational Drugs

0.1 N NaOH 42.0-43.8 (mg/mL)

- NCI Investigational Drugs

35% Ethyl alcohol 14.2-15.0 (mg/mL)

- NCI Investigational Drugs

### 4.2.5 LogP

-3.5

- DrugBank

-2.17 (LogP)

*SANGSTER (1994)*

- EPA DSSTox

-3.5

- Human Metabolome Database (HMDB)

### 4.2.6 Stability/Shelf Life

Intact vials should be stored under refrigeration & are stable for a least 4 yr. Although the drug is stable for 3 yr at room temp, refrigeration is recommended because degradation may result at elevated temperatures. The constituted soln hydrolyzes at room temp & should be used within 30 min. The pH providing optimum soln stability has been reported to be about 6.5-7. Azacitidine 0.5 & 2 mg/ml in Ringer's injection, lactated, was stable for up to one month when frozen at -20 °C in polypropylene syringes.

*Trissel, L.A. Handbook on Injectable Drugs. 9th ed. Bethesda, MD. American Society of Health-System Pharmacists' Product Development. 1996., p. 1143*

- Hazardous Substances Data Bank (HSDB)

**Stability**

Bulk: Samples of 5- azacitidine and 5- azacitidine hydrate were found to be stable at 25 °C and 60 °C for at least 30 days. Solution: Dilute aqueous solutions of 5-azacitidine have been found to be unstable at 24 -26 ° C. A 1% aqueous solution at 5-6°C decomposes 2, 5, and 9% in 2, 8, and 24 hours respectively. At room temperature a 1% aqueous solution shows 7, 20 and 41% decomposition in 2, 8, and 24 hours respectively (UV and NMR).

- NCI Investigational Drugs

### 4.2.7 Optical Rotation

Optical rotation: + 39 degrees @ 25 °C (c = 1 in water)

*Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 153*

- Hazardous Substances Data Bank (HSDB)

(c = 1, H2O) [a]20 D = 40.0 ± 1.0°

NCI Investigational Drugs

### 4.2.8 Decomposition

When heated to decomposition it emits toxic fumes of /nitrogen oxides/.

*Gleason, M.N., R.E. Gosselin, H.C. Hodge, and R.P. Smith. Clinical Toxicology of Commercial Products. 3rd ed. Baltimore: Williams and Wilkins, 1969., p. 296*

Hazardous Substances Data Bank (HSDB)

# 5 Spectral Information

## 5.1 1D NMR Spectra

| | |
|---|---|
| 1D NMR Spectra | NMRShiftDB Link |

▸ NMRShiftDB

### 5.1.1 1H NMR Spectra

| | |
|---|---|
| Spectra ID | 2335 |
| Instrument Type | JEOL |
| Frequency | 400 MHz |
| Solvent | DMSO-d6 |
| Shifts [ppm]:Intensity | 3.54:176.00, 3.55:185.00, 3.57:237.00, 3.58:225.00, 3.68:214.00, 3.69:234.00, 3.71:156.00, 3.72:155.00, 3.85:218.00, 3.86:207.00, 3.87:250.00, 4.00:185.00, 4.02:312.00, 4.03:216.00, 4.08:234.00, 4.09:292.00, 4.10:176.00, 5.67:469.00, 5.68:460.00, 7.53:281.00, 7.54:237.00, 8.59:1000.00 |
| Thumbnail | |

▸ Human Metabolome Database (HMDB)

| | |
|---|---|
| Source of Spectrum | Sigma-Aldrich Co. LLC. |
| Source of Sample | Sigma-Aldrich Co. LLC. |
| Catalog Number | 852880 |
| Copyright | Copyright © 2021 Sigma-Aldrich Co. LLC. - Database Compilation Copyright © 2021 John Wiley & Sons, Inc. All Rights Reserved. |
| Thumbnail | |

▸ SpectraBase

### 5.1.2 13C NMR Spectra

| | |
|---|---|
| Spectra ID | 3035 |
| Instrument Type | JEOL |
| Frequency | 22.53 MHz |
| Solvent | DMSO-d6 |
| Shifts [ppm]:Intensity | 153.19:579.00, 156.24:783.00, 165.75:947.00, 60.15:667.00, 68.96:907.00, 73.83:1000.00, 84.31:813.00, 89.29:830.00 |
| Thumbnail | |

▸ Human Metabolome Database (HMDB)

| | |
|---|---|
| **Source of Spectrum** | Sigma-Aldrich Co. LLC. |
| **Source of Sample** | Sigma-Aldrich Co. LLC. |
| **Catalog Number** | 852880 |
| **Copyright** | Copyright © 2021 Sigma-Aldrich Co. LLC. - Database Compilation Copyright © 2021 John Wiley & Sons, Inc. All Rights Reserved. |
| **Thumbnail** | |

▸ SpectraBase

## 5.2 UV Spectra

UV max (water): 241 nm (epsilon 8767); (0.01 N HCl): 249 nm (epsilon 3077); (0.01 N KOH): 223 nm (epsilon 24200)

*Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 153*

▸ Hazardous Substances Data Bank (HSDB)

(0.1 M acetate buffer, pH 5) max = 242 ±2nm E = 6,850 - 7,250

▸ NCI Investigational Drugs

## 5.3 IR Spectra

### 5.3.1 ATR-IR Spectra

| | |
|---|---|
| **Instrument Name** | Bio-Rad FTS |
| **Technique** | ATR-Neat (DuraSamplIR II) |
| **Source of Spectrum** | Forensic Spectral Research |
| **Source of Sample** | Sigma-Aldrich Company Llc |
| **Catalog Number** | A2385 |
| **Lot Number** | SLBD1299V |
| **Copyright** | Copyright © 2012-2021 John Wiley & Sons, Inc. All Rights Reserved. |
| **Thumbnail** | |

SpectraBase

| | |
|---|---|
| **Source of Sample** | Aldrich |
| **Catalog Number** | 852880 |
| **Copyright** | Copyright © 2018-2021 Sigma-Aldrich Co. LLC. - Database Compilation Copyright © 2018-2021 John Wiley & Sons, Inc. All Rights Reserved. |
| **Thumbnail** | |

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## 5.4 Chromatograms

### 5.4.1 HPLC

| | |
|---|---|
| **HPLC** | Column: Alltech C8 300 mm x 4.6 mm i.d. Mobile Phase: pH 6.5, 0.02 M KH Flow Rate: 1.5 mL/min Detection: UV at 210 nm Sample Preparation: 0.5 mg of the sample is quickly dissolved in 1.0 mL of the mobile phase or internal standard solution Internal Standard: **Uridine** (1.5 mg/mL in mobile phase) Retention Volume: 6.8 mL (NSC - 102816) 9.0 mL (I.S) |

NCI Investigational Drugs

## 5.5 Raman Spectra

| | |
|---|---|
| **Technique** | FT-Raman |
| **Source of Spectrum** | Forensic Spectral Research |
| **Source of Sample** | Sigma-Aldrich Company Llc |
| **Catalog Number** | A2385 |
| **Lot Number** | SLBD1299V |
| **Copyright** | Copyright © 2013-2021 John Wiley & Sons, Inc. All Rights Reserved. |
| **Thumbnail** | |

SpectraBase

# 6 Related Records

## 6.1 Related Compounds with Annotation

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## 6.2 Related Compounds

| | |
|---|---|
| Same Connectivity | 57 Records |
| Same Stereo | 7 Records |
| Same Isotope | 34 Records |
| Same Parent, Connectivity | 99 Records |
| Same Parent, Stereo | 36 Records |
| Same Parent, Isotope | 76 Records |
| Same Parent, Exact | 30 Records |
| Mixtures, Components, and Neutralized Forms | 98 Records |
| Similar Compounds | 330 Records |
| Similar Conformers | 4,715 Records |

PubChem

## 6.3 Substances

### 6.3.1 Related Substances

| | |
|---|---|
| All | 424 Records |
| Same | 276 Records |
| Mixture | 148 Records |

PubChem

### 6.3.2 Substances by Category

PubChem

## 6.4 Entrez Crosslinks

| | |
|---|---|
| PubMed | 3,301 Records |
| Protein Structures | 1 Record |
| Taxonomy | 5 Records |
| OMIM | 30 Records |
| Gene | 443 Records |

PubChem

## 6.5 NCBI LinkOut

NCBI

## 7 Chemical Vendors

PubChem

# 8 Drug and Medication Information

## 8.1 Drug Indication

Showing 3 of 10 View More

For treatment of patients with the following French-American-British myelodysplastic syndrome subtypes: refractory anemia or refractory anemia with ringed sideroblasts (if accompanied by neutropenia or thrombocytopenia or requiring transfusions), refractory anemia with excess blasts, refractory anemia with excess blasts in transformation (now classified as acute myelogenous leukemia with multilineage dysplasia), and chronic myelomonocytic leukemia.

- DrugBank

FDA Label

- DrugBank

Azacitidine Mylan is indicated for the treatment of adult patients who are not eligible for haematopoietic stem cell transplantation (HSCT) with:intermediate 2 and high risk myelodysplastic syndromes (MDS) according to the International Prognostic Scoring System (IPSS),chronic myelomonocytic leukaemia (CMML) with 10 29% marrow blasts without myeloproliferative disorder,acute myeloid leukaemia (AML) with 20 30% blasts and multi lineage dysplasia, according to World Health Organisation (WHO) classification,AML with > 30% marrow blasts according to the WHO classification.

- European Medicines Agency (EMA)

## 8.2 LiverTox Summary

Azacitidine is a cytosine analogue and antineoplastic agent used in the therapy of myelodysplastic syndromes. Azacitidine is associated with a low rate of transient serum enzyme elevations during therapy and has only rarely been implicated in cases of clinically apparent acute liver injury with jaundice.

- LiverTox

## 8.3 Drug Classes

Antineoplastic Agents

- LiverTox

## 8.4 Drug Effects during Lactation

| | |
|---|---|
| **Summary** | Most sources consider breastfeeding to be contraindicated during maternal antineoplastic drug therapy. It might be possible to breastfeed safely during intermittent azacitidine therapy with an appropriate period of breastfeeding abstinence; the manufacturer recommends an abstinence period of 1 week after the last dose. Chemotherapy may adversely affect the normal microbiome and chemical makeup of breastmilk. Women who receive chemotherapy during pregnancy are more likely to have difficulty nursing their infant. |
| **PubMed** | 30000021 |
| **NCBI Books** | NBK500962 |

- Drugs and Lactation Database (LactMed)

## 8.5 FDA Orange Book

- FDA Orange Book

## 8.6 FDA National Drug Code Directory

National Drug Code (NDC) Directory

AZACITIDINE is an active ingredient in 4 products including: 'AZACITIDINE FOR', AZACITIDINE, and ONUREG.

National Drug Code (NDC) Directory

## 8.7 Drug Labels for Ingredients

| | |
|---|---|
| **Label Information** | Total 25 labels |
| **Drug Ingredient** | AZACITIDINE |
| **NDC Code(s)** | 0143-9606-01, 0781-3253-94, 0781-9253-94, 16714-927-01, 16729-306-10, 43598-305-62, 43598-465-62, 43598-678-11, 43817-906-01, 51991-797-98, 59572-102-01, 59572-730-07, 59572-730-14, 59572-740-07, 59572-740-14, 63323-771-39, 64679-096-01, 67457-254-30, 68001-313-56, 68001-504-54, 68001-527-54, 69097-368-40, 69097-805-40, 70121-1237-1, 71288-115-30, 71288-153-95, 72485-201-01, 72606-558-01 |
| **Packagers** | Accord Healthcare Inc.; Amneal Pharmaceuticals LLC; Armas Pharmaceuticals Inc.; BluePoint Laboratories; Breckenridge Pharmaceutical, Inc.; CELLTRION USA, INC.; Celgene Corporation; Cipla USA Inc.; Dr. Reddy's Laboratories Inc.; Fresenius Kabi USA, LLC; Hikma Pharmaceuticals USA Inc.; Meitheal Pharmaceuticals Inc.; Mylan Institutional LLC; NorthStar RxLLC; Panacea Biotec Limited; Sandoz Inc; Wockhardt USA LLC. |

DailyMed

## 8.8 Clinical Trials

### 8.8.1 ClinicalTrials.gov

ClinicalTrials.gov

### 8.8.2 EU Clinical Trials Register

EU Clinical Trials Register

### 8.8.3 NIPH Clinical Trials Search of Japan

NIPH Clinical Trials Search of Japan

## 8.9 EMA Drug Information

Showing 2 of 7 View More

| | |
|---|---|
| **Medicine** | Azacitidine Mylan |
| **Therapeutic area** | Myelodysplastic Syndromes; Leukemia, Myelomonocytic, Chronic; Leukemia, Myeloid, Acute |
| **Active Substance** | azacitidine |
| **INN/Common name** | azacitidine |
| **Pharmacotherapeutic Classes** | Antineoplastic agents |
| **Status** | This medicine is authorized for use in the European Union |
| **Company** | Mylan Ireland Limited |
| **Market Date** | 2020-03-27 |

European Medicines Agency (EMA)

| | |
|---|---|
| **Medicine** | Azacitidine betapharm |
| **Therapeutic area** | Myelodysplastic Syndromes; Leukemia, Myelomonocytic, Chronic; Leukemia, Myeloid, Acute |
| **Active Substance** | azacitidine |
| **INN/Common name** | azacitidine |
| **Pharmacotherapeutic Classes** | Antineoplastic agents |
| **Status** | This medicine is authorized for use in the European Union |
| **Company** | betapharm Arzneimittel GmbH |
| **Market Date** | 2020-03-24 |

European Medicines Agency (EMA)

## 8.10 Therapeutic Uses

Anticancer agent used to treat acute myelogenous leukemia

*Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V5 (1993) 872*

Hazardous Substances Data Bank (HSDB)

Expl Ther: The ability of phenylacetate to prevent carcinogenesis by the chemotherapeutic hypomethylating drug 5-aza-2'-deoxycytidine (5AzadC) was tested in vitro and in mice. Transient exposure of immortalized, but poorly tumorigenic ras-transformed 4C8 fibroblasts to 5AzadC resulted in neoplastic transformation manifested by loss of contact inhibition of growth, acquired invasiveness, and increased tumorigenicity in athymic mice.

*Prasanna P et al; Clin Cancer Res 1 (8): 865-71*

Hazardous Substances Data Bank (HSDB)

5-Azacytidine, an inhibitor of DNA methylation as well as a cytidine antimetabolite, becomes incorporated predominantly into RNA and has antileukemic and differentiating action. A newer analog, 2',2'-difluorodeoxycytidine (gemcitabine), becomes incorporated into DNA and inhibits the elongation of nascent DNA strands. It has promising activity in various human solid tumors, including lung cancer and ovarian cancer ... .

*Hardman, J.G., L.E. Limbird, P.B. Molinoff, R.W. Ruddon, A.G. Goodman (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 9th ed. New York, NY: McGraw-Hill, 1996., p. 1249*

Hazardous Substances Data Bank (HSDB)

# 9 Pharmacology and Biochemistry

## 9.1 Pharmacodynamics

Azacitidine is believed to exert its antineoplastic effects by causing hypomethylation of DNA and direct cytotoxicity on abnormal hematopoietic cells in the bone marrow. The concentration of azacitidine required for maximum inhibition of DNA methylation in vitro does not cause major suppression of DNA synthesis. Hypomethylation may restore normal function to genes that are critical for differentiation and proliferation. The cytotoxic effects of azacitidine cause the death of rapidly dividing cells, including cancer cells that are no longer responsive to normal growth control mechanisms. Non-proliferating cells are relatively insensitive to azacitidine. Upon uptake into cells, azacitidine is phosphorylated to 5-azacytidine monophosphate by uridine-cytidine kinase, then to diphosphate by pyrimidine monophosphate kinases and triphosphate by diphosphate kinases. 5-Azacitidine triphosphate is incorporated into RNA, leading to the disruption of nuclear and cytoplasmic RNA metabolism and inhibition of protein synthesis. 5-Azacytidine diphosphate is reduced to 5-aza-deoxycytidine diphosphate by ribonucleotide reductase. The resultant metabolite is phosphorylated to 5-azadeoxycitidine triphosphate by nucleoside diphosphate kinases. 5-azadeoxycitidine triphosphate is then incoporated into DNA, leading to inhibition of DNA synthesis. Azacitidine is most toxic during the S-phase of the cell cycle.

- DrugBank

## 9.2 MeSH Pharmacological Classification

**Enzyme Inhibitors**

Compounds or agents that combine with an enzyme in such a manner as to prevent the normal substrate-enzyme combination and the catalytic reaction. (See all compounds classified as Enzyme Inhibitors.)

- Medical Subject Headings (MeSH)

**Antimetabolites, Antineoplastic**

Antimetabolites that are useful in cancer chemotherapy. (See all compounds classified as Antimetabolites, Antineoplastic.)

- Medical Subject Headings (MeSH)

## 9.3 FDA Pharmacological Classification

| | |
|---|---|
| **FDA UNII** | M801H13NRU |
| **Active Moiety** | AZACITIDINE |
| **Pharmacological Classes** | Mechanisms of Action [MoA] - Nucleic Acid Synthesis Inhibitors |
| **Pharmacological Classes** | Established Pharmacologic Class [EPC] - Nucleoside Metabolic Inhibitor |
| **FDA Pharmacology Summary** | Azacitidine is a Nucleoside Metabolic Inhibitor. The mechanism of action of azacitidine is as a Nucleic Acid Synthesis Inhibitor. |

- FDA Pharm Classes

| | |
|---|---|
| **Non-Proprietary Name** | AZACITIDINE |
| **Pharmacological Classes** | Nucleoside Metabolic Inhibitor [EPC]; Nucleic Acid Synthesis Inhibitors [MoA] |

- National Drug Code (NDC) Directory

## 9.4 ATC Code

L01BC07

- European Medicines Agency (EMA); NORMAN Suspect List Exchange

L - Antineoplastic and immunomodulating agents

L01 - Antineoplastic agents

L01B - Antimetabolites

L01BC - Pyrimidine analogues

L01BC07 - Azacitidine

- WHO Anatomical Therapeutic Chemical (ATC) Classification

## 9.5 Absorption, Distribution and Excretion

**Absorption**

Azacitidine is rapidly absorbed after subcutaneous administration. The bioavailability of subcutaneous azacitidine relative to IV azacitidine is approximately 89%, based on area under the curve.

- DrugBank

**Route of Elimination**

Following IV administration of radioactive azacitidine to 5 cancer patients, the cumulative urinary excretion was 85% of the radioactive dose. Fecal excretion accounted for <1% of administered radioactivity over three days. Mean excretion of radioactivity in urine following SC administration of 14C-azacitidine was 50%.

DrugBank

**Volume of Distribution**

76 ± 26 L

DrugBank

**Clearance**

167 +/- 49 L/h

DrugBank

## 9.6 Metabolism/Metabolites

An in vitro study of azacitidine incubation in human liver fractions indicated that azacitidine may be metabolized by the liver. The potential of azacitidine to inhibit cytochrome P450 (CYP) enzymes is not known.

DrugBank

## 9.7 Biological Half-Life

Mean elimination half-life is approximately 4 hours.

DrugBank

## 9.8 Mechanism of Action

Azacitidine (5-azacytidine) is a chemical analogue of the cytosine nucleoside used in DNA and RNA. Azacitidine may induce antineoplastic activity by inhibition of DNA methyltransferase at low doses and cytotoxicity through incorporation into RNA and DNA at high doses. Covalent binding to DNA methyltransferase results in hypomethylation of DNA and prevents DNA synthesis. As azacitidine is a ribonucleoside, it incoporates into RNA to a larger extent than into DNA. The incorporation into RNA leads to the dissembly of polyribosomes, defective methylation and acceptor function of transfer RNA, and inhibition of the production of protein, resulting in cell death.

DrugBank

Telomerase activation is thought to be a critical step in cellular immortality and oncogenesis. Several reagents including differentiation-inducing and antineoplastic agents are known to inhibit telomerase activity, although the molecular mechanisms through which they inhibit telomerase activity remain unclear. Demethylating reagents have recently been used as potential antineoplastic drugs for some types of cancers including those of the prostate. In the present study, we examined the effect of the demethylating reagent 5-azacytidine (5-aza-CR) on telomerase activity using cells of two prostate cancer cell lines, DU-145 and TSU-PR1. 5-aza-CR treatment significantly reduced telomerase activity in TSU-PR1 cells, but not in DU-145 cells, although growth inhibition was observed to a similar extent in both cell lines. Reverse transcription-PCR analyses revealed that inhibition of telomerase activity was accompanied by down-regulation of telomerase catalytic subunit (hTERT) mRNA expression. Transient expression assays showed that 5-aza-CR repressed the transcriptional activity of the hTERT promoter and that the E-box within the core promoter was responsible for this down-regulation. Western blot analyses revealed that 5-aza-CR reactivated p16 expression and repressed c-Myc expression in TSU-PR1 cells but not in DU-145 cells. Overexpression of p16 in TSU-PR1 cells led to significant repression of c-Myc transcription. These findings suggest that 5-aza-CR inhibits telomerase activity via transcriptional repression of hTERT, in which p16 and c-Myc may play a key role.

*PMID:10914736*

*Kitagawa Y et al; Clin cancer Res 6 (7): 2868-75 (2000)*

Hazardous Substances Data Bank (HSDB)

Cellular differentiation is controlled by a variety of factors including gene methylation, which represses particular genes as cell fate is determined. The incorporation of 5-azacytidine (5azaC) into DNA in vitro prevents methylation and thus can alter cellular differentiation pathways. Human bone marrow fibroblasts and MG63 cells treated with 5azaC were used as models of osteogenic progenitors and of a more mature osteoblast phenotype, respectively. The capacity for differentiation of these cells following treatment with glucocorticoids was investigated. 5azaC treatment led to significant expression of the osteoblastic marker alkaline phosphatase in MG63 osteosarcoma cells, which was further augmented by glucocorticoids; however, in human marrow fibroblasts alkaline phosphatase activity was only observed in glucocorticoid-treated cultures. MG63 cells represent a phenotype late in the osteogenic lineage in which demethylation is sufficient to induce alkaline phosphatase activity. Marrow fibroblasts are at an earlier stage of differentiation and require stimulation with glucocorticoids. In contrast, the expression of osteocalcin, an osteoblastic marker, was unaffected by 5azaC treatment, suggesting that regulation of expression of the osteocalcin gene does not involve methylation. These models provide novel approaches to the study of the control of differentiation in the marrow fibroblastic system.

*Locklin RM et al; Cell Biol Int 22 (3): 207-15*

Hazardous Substances Data Bank (HSDB)

## 9.9 Human Metabolite Information

### 9.9.1 Cellular Locations

Cytoplasm

Human Metabolome Database (HMDB)

# 10 Use and Manufacturing

## 10.1 Uses

Anticancer agent used to treat acute myclogenous leukemia

*Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V5 (1993) 872*

- Hazardous Substances Data Bank (HSDB)

### 10.1.1 Use Classification

Human drugs -> Azacitidine Mylan -> EMA Drug Category

- European Medicines Agency (EMA)

Antineoplastic agents -> Human pharmacotherapeutic group

- European Medicines Agency (EMA)

Human drugs -> Azacitidine betapharm -> EMA Drug Category

- European Medicines Agency (EMA)

Human drugs -> Azacitidine Accord -> EMA Drug Category

- European Medicines Agency (EMA)

Human drugs -> Azacitidine Celgene -> EMA Drug Category

- European Medicines Agency (EMA)

Human drugs -> Vidaza -> EMA Drug Category

- European Medicines Agency (EMA)

Human Drugs -> EU pediatric investigation plans

- European Medicines Agency (EMA)

Human drugs -> Onureg -> EMA Drug Category

- European Medicines Agency (EMA)

Human Drugs -> FDA Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) -> Active Ingredients

- FDA Orange Book

## 11 Identification

### 11.1 Analytic Laboratory Methods

AOAC Method 973.30. Polycyclic Aromatic Hydrocarbons and Benzo(a)pyrene in Food.. Spectrophotometric method. /Polycyclic aromatic hydrocarbons/

*Association of Official Analytical Chemists. Official Methods of Analysis. 15th ed. and Supplements. Washington, DC: Association of Analytical Chemists, 1990, p. 1176*

Hazardous Substances Data Bank (HSDB)

# 12 Safety and Hazards

## 12.1 Hazards Identification

### 12.1.1 GHS Classification

| | |
|---|---|
| **Pictogram(s)** |  Irritant Health Hazard |
| **Signal** | Danger |
| **GHS Hazard Statements** | H302: Harmful if swallowed [Warning Acute toxicity, oral]<br>H341: Suspected of causing genetic defects [Warning Germ cell mutagenicity]<br>H350: May cause cancer [Danger Carcinogenicity]<br>H360: May damage fertility or the unborn child [Danger Reproductive toxicity]<br>H372: Causes damage to organs through prolonged or repeated exposure [Danger Specific target organ toxicity, repeated exposure] |
| **Precautionary Statement Codes** | P203, P260, P264, P270, P280, P281, P301+P317, P318, P319, P330, P405, and P501<br>(The corresponding statement to each P-code can be found at the GHS Classification page.) |

NITE-CMC

### 12.1.2 Hazard Classes and Categories

Acute toxicity (Oral) - Category 4

Germ cell mutagenicity - Category 2

Carcinogenicity - Category 1B

Reproductive toxicity - Category 1B

Specific target organ toxicity - Repeated exposure - Category 1 (blood system, liver)

NITE-CMC

### 12.1.3 Health Hazards

SYMPTOMS: Symptoms of exposure to this compound via intravenous route include nausea, vomiting, diarrhea, reduction in white cell count, leukopenia and agranulocytosis. Other symptoms via intravenous route include dose-related leukemia, thrombocytopenia, myelosuppression, gastrointestinal upset, alterations in hepatic function tests, fatal hepatic coma, myalgia, rhabdomyolysis, rash, stomatitis, fever, hypotension and reversible renal impairment. Symptoms of exposure to this type of compound include anorexia, local irritant effects, allergic reactions including pruritus and erythema, headache, malaise, weakness, anaphylaxis, vesicant or irritant effect on skin and mucous membranes, thrombophlebitis, anemia, bleeding, immunosuppressant effect, mouth ulcers, esophagitis, abdominal pain, hemorrhage, perforation of the stomach, alopecia, delayed wound healing, amenorrhea, inhibition of spermatogenesis, gynecomastia, hyperuricemia, acute renal failure due to uric acid nephropathy, hyperphosphatemia, disturbances of electrolyte balance, pigmentation of the skin and nails, jaundice and abnormal liver function tests. ACUTE/CHRONIC HAZARDS: This compound is harmful if swallowed, inhaled or absorbed through the skin. It may cause irritation. When heated to decomposition it emits toxic fumes of carbon monoxide, carbon dioxide and nitrogen oxides. (NTP, 1992)

*National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.*

CAMEO Chemicals

### 12.1.4 Fire Hazards

Flash point data for this chemical are not available; however, it is probably combustible. (NTP, 1992)

*National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.*

CAMEO Chemicals

### 12.1.5 Skin, Eye, and Respiratory Irritations

A skin irritant.

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 295*

Hazardous Substances Data Bank (HSDB)

## 12.2 First Aid Measures

### 12.2.1 First Aid

EYES: First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center. Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician. IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop. SKIN: IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water. If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment. INHALATION: IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. IMMEDIATELY call a physician and be prepared to transport the victim to a hospital even if no symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop. Provide proper respiratory protection to rescuers

entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Protective Clothing. INGESTION: DO NOT INDUCE VOMITING. If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician. If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital. OTHER: Since this chemical is a known or suspected carcinogen you should contact a physician for advice regarding the possible long term health effects and potential recommendation for medical monitoring. Recommendations from the physician will depend upon the specific compound, its chemical, physical and toxicity properties, the exposure level, length of exposure, and the route of exposure. (NTP, 1992)

*National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.*

▸ CAMEO Chemicals

## 12.3 Fire Fighting

Fires involving this material can be controlled with a dry chemical, carbon dioxide or Halon extinguisher. A water spray may also be used. (NTP, 1992)

*National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.*

▸ CAMEO Chemicals

## 12.4 Accidental Release Measures

### 12.4.1 Disposal Methods

SRP: At the time of review, criteria for land treatment or burial (sanitary landfill) disposal practices are subject to significant revision. Prior to implementing land disposal of waste residue (including waste sludge), consult with environmental regulatory agencies for guidance on acceptable disposal practices.

▸ Hazardous Substances Data Bank (HSDB)

## 12.5 Handling and Storage

### 12.5.1 Nonfire Spill Response

SMALL SPILLS AND LEAKAGE: If you spill this chemical, you should dampen the solid spill material with water, then transfer the dampened material to a suitable container. Use absorbent paper dampened with water to pick up any remaining material. Seal your contaminated clothing and the absorbent paper in a vapor-tight plastic bag for eventual disposal. Wash all contaminated surfaces with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned. STORAGE PRECAUTIONS: You should protect this chemical from exposure to light. Keep the container tightly closed under an inert atmosphere, and store under refrigerated temperatures. (NTP, 1992)

*National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.*

▸ CAMEO Chemicals

### 12.5.2 Storage Conditions

Intact vials should be stored under refrigeration & are stable for a least 4 yr. Although the drug is stable for 3 yr at room temp, refrigeration is recommended because degradation may result at elevated temperatures. The constituted soln hydrolyzes at room temp & should be used within 30 min. ... Azacitidine 0.5 & 2 mg/ml in Ringer's injection, lactated, was stable for up to one month when frozen at -20 °C in polypropylene syringes.

*Trissel, L.A. Handbook on Injectable Drugs. 9th ed. Bethesda, MD. American Society of Health-System Pharmacists' Product Development. 1996., p. 1143*

▸ Hazardous Substances Data Bank (HSDB)

## 12.6 Exposure Control and Personal Protection

### 12.6.1 Personal Protective Equipment (PPE)

RECOMMENDED RESPIRATOR: Where the neat test chemical is weighed and diluted, wear a NIOSH-approved half face respirator equipped with a combination filter cartridge, i.e. organic vapor/acid gas/HEPA (specific for organic vapors, HCl, acid gas, SO2 and a high efficiency particulate filter). (NTP, 1992)

*National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.*

▸ CAMEO Chemicals

## 12.7 Stability and Reactivity

### 12.7.1 Air and Water Reactions

Slightly water soluble. Unstable in solution.

▸ CAMEO Chemicals

### 12.7.2 Reactive Group

Alcohols and Polyols

Amides and Imides

Amines, Phosphines, and Pyridines

CAMEO Chemicals

### 12.7.3 Reactivity Profile

5-AZACYTIDINE is sensitive to light (may discolor). It is sensitive to oxidation. It is unstable in solution. It undergoes hydrolysis in aqueous buffers. This chemical is incompatible with strong oxidizers. (NTP, 1992)

*National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina.*

CAMEO Chemicals

## 12.8 Other Safety Information

### 12.8.1 Special Reports

National Toxicology Program. Eleventh Report on Carcinogens (2005). The Report on Carcinogens is an informational scientific and public health document that identifies and discusses substances (including agents, mixtures, or exposure circumstances) that may pose a carcinogenic hazard to human health. Azacitidine (320-67-2) is listed as reasonably anticipated to be a human carcinogen.[Available from, as of July 31, 2009: http://ntp.niehs.nih.gov/ntp/roc/eleventh/profiles/s017azac.pdf]

Hazardous Substances Data Bank (HSDB)

# 13 Toxicity

## 13.1 Toxicological Information

### 13.1.1 Toxicity Summary

One case of overdose with azacitidine was reported during clinical trials. A patient experienced diarrhea, nausea, and vomiting after receiving a single IV dose of approximately 290 mg/m2, almost 4 times the recommended starting dose.

DrugBank

### 13.1.2 Hepatotoxicity

In clinical trials, serum enzyme elevations occurred in up to 16% of patients on azacitidine therapy for cancer or myelodysplasia who had concurrent, underlying liver disease or liver metastases, but rarely in persons without a preexisting hepatic illness. In subsequent studies, liver adverse reactions attributed to azacitidine have rarely been reported, at least when it is given in conventional doses. Nevertheless, monitoring of serum enzyme levels is recommended in treating patients who have concurrent liver disease. Cases of clinically apparent liver injury attributed to azacitidine in patients without underlying liver disease have not been reported in the literature.

Likelihood score: E* (unproven but suspected cause of clinically apparent liver injury in persons with pre-existing liver disease).

LiverTox

### 13.1.3 Drug Induced Liver Injury

| | |
|---|---|
| **Compound** | azacitidine |
| **DILI Annotation** | Ambiguous DILI-concern |
| **Severity Grade** | 8 |
| **Label Section** | Warnings and precautions |
| **References** | M Chen, V Vijay, Q Shi, Z Liu, H Fang, W Tong. FDA-Approved Drug Labeling for the Study of Drug-Induced Liver Injury, Drug Discovery Today, 16(15-16):697-703, 2011. PMID:21624500 DOI:10.1016/j.drudis.2011.05.007<br>M Chen, A Suzuki, S Thakkar, K Yu, C Hu, W Tong. DILIrank: the largest reference drug list ranked by the risk for developing drug-induced liver injury in humans. Drug Discov Today 2016, 21(4): 648-653. PMID:26948801 DOI:10.1016/j.drudis.2016.02.015 |

Drug Induced Liver Injury Rank (DILIrank) Dataset

### 13.1.4 Evidence for Carcinogenicity

Azacitidine: reasonably anticipated to be a human carcinogen.

*DHHS/National Toxicology Program; Eleventh Report on Carcinogens: Azacitidine (320-67-2) (January 2005). Available from, as of July 31, 2009: **https://ntp.niehs.nih.gov/ntp/roc/eleventh/profiles/s017azac.pdf***

Hazardous Substances Data Bank (HSDB)

### 13.1.5 Carcinogen Classification

| | |
|---|---|
| **IARC Carcinogenic Agent** | Azacitidine |
| **IARC Carcinogenic Classes** | Group 2A: Probably carcinogenic to humans |
| **IARC Monographs** | Volume 50: (1990) Pharmaceutical Drugs |

International Agency for Research on Cancer (IARC)

### 13.1.6 Acute Effects

ChemIDplus

### 13.1.7 Toxicity Data

**ToxicityData**

Woman(iv): TDLo,: 500 ,ug/kg

*Cancer Chemotherapy Reports, 56,413,(1972)*

NCI Investigational Drugs

**ToxicityData**

Mouse(po): LD50: 572 mg/kg

*Toxicology and Applied Pharmacology, 19,382,(1971)*

NCI Investigational Drugs

**ToxicityData**

Mouse(ip): LD50: 68 mg/kg

*Experientia, 22,53,(1966)*

NCI Investigational Drugs

**ToxicityData**

Mouse(iv): LD50: 229 mg/kg

*National Technical Information Service, PB84- 211432*

NCI Investigational Drugs

**ToxicityData**

Dog(iv): LD50: 7200 ug/kg

*Advances in Pharmacology and Chemotherapy,14,285,(1977)*

NCI Investigational Drugs

### 13.1.8 Antidote and Emergency Treatment

Basic treatment: Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if needed. Administer **oxygen** by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary ... . Monitor for shock and treat if necessary ... . Anticipate seizures and treat if necessary ... . For eye contamination, flush eyes immediately with **water**. Irrigate each eye continuously with **normal saline** during transport ... . Do not use emetics. For ingestion, rinse mouth and administer 5 ml/kg up to 200 ml of **water** for dilution if the patient can swallow, has a strong gag reflex, and does not drool ... . Cover skin burns with dry sterile dressings after decontamination ... . /Poison A and B/

*Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994., p. 139*

Hazardous Substances Data Bank (HSDB)

Advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious, has severe pulmonary edema, or is in respiratory arrest. Positive pressure ventilation techniques with a bag valve mask device may be beneficial. Monitor cardiac rhythm and treat arrhythmias as necessary ... . Start an IV with D5W /SRP: "To keep open", minimal flow rate/. Use lactated Ringer's if signs of hypovolemia are present. Watch for signs of fluid overload. Consider drug therapy for pulmonary edema ... . For hypotension with signs of hypovolemia, administer fluid cautiously. Watch for signs of fluid overload ... . Treat seizures with **diazepam (Valium)** ... . Use **proparacaine hydrochloride** to assist eye irrigation ... . /Poison A and B/

*Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994., p. 139*

Hazardous Substances Data Bank (HSDB)

### 13.1.9 Human Toxicity Excerpts

Human systemic effects by iv route: nausea, vomiting & diarrhea, reduction in white cell count (leukopenia & agranulocytosis).

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 295*

Hazardous Substances Data Bank (HSDB)

Acute Toxicity: Nausea & vomiting; diarrhea; fever; rash; drowsiness. Delayed Toxicity: Bone marrow depression; hepatic damage; muscle pain & weakness; possibly cardiotoxicity. /From table/

*Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997., p. 1324*

Hazardous Substances Data Bank (HSDB)

A skin irritant.

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 295*

Hazardous Substances Data Bank (HSDB)

... Treated human cells, in which separation does not depend upon the quantity of heterochromatin, /was coducted/ with 2x10(-5) and 6x10(-6) M **5-AC** for 5 and 8 hr. Compared with the control, **5-AC** treatment resulted in an increased frequency of separated centromeres of acrocentric chromosomes in relation to those of non-acrocentric chromosomes. In the control the acrocentric chromosomes are the last to separate; in the treated population there was almost random separation of the two types of chromosomes. This epigenetic alteration might be another factor which results in genesis of aneuploidy.

***PMID:11230551***

*Rodriguez MJ et al; Mutagenesis 16 (2): 109-14 (2001)*

Hazardous Substances Data Bank (HSDB)

High dose azacitidine causes renal dysfunction manifested by tubular acidosis, polyuria and increased urinary excretion of electrolytes, glucose and amino acids.

PMID:11219485

*Kintzel PE; Drug Saf 24 (1): 19-38 (2001)*

Hazardous Substances Data Bank (HSDB)

### 13.1.10 Non-Human Toxicity Excerpts

An experimental teratogen. Other experimental reproductive effects.

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 295*

Hazardous Substances Data Bank (HSDB)

DNA methylation is an epigenetical mechanism that plays crucial roles in cellular differentiation and tissue development in embryogenesis. The aim of the present study was to determine the effects of a demethylating agent, 5-azacytidine, on testicular development during embryonal life in mouse. Ten pregnant mice were administered 5-azacytidine (5-azaC) (ip 2 mg/kg of agent dissolved in 0.1 mg/ml PBS) during 8th (Group 1), 11th (Group 2), 14th (Group 3) and 18th (Group 4) days of pregnancy periods and male siblings of these animals were obtained (experimental groups) whereas the control group animals received no treatment and siblings of this group were also obtained. Testicular tissues from all groups were taken 20 days after birth and examined at the light and electron microscopical levels. All pregnancies were terminated in Group 1 animals, therefore no observations could be done in this group. While Group 2 and 3 siblings showed distinctive kongenital abnormalities such as; anancephaly, growth failure, cleft palate, extremity abnormalities, supernumerary ribs and whirled shaped-tails, no such abnormalities were observed in Group 4 when compared to the control group. Microscopical examination of testicular tissues in groups 2 and 3 demonstrated cellular disintegration of spermatocytes in seminiferous tubules. In addition, cytoplasmic vacuoles and thickening of the basement membrane were also evident in both groups 2 and 3. Apoptotic-like cells were seen especially in group 2 and rarely in group 3. There were no structural alterations in group 4 animals, except a decreased number of spermatocytes in seminiferous tubules when compared to the control group, possibly indicating the completion of embryogenesis in this group. In conclusion, it could be suggested that the demethylating agent 5-azacytidine may trigger an unknown gene reactivation during early embryogenesis possibly affecting the cell and tissue differentiation in developing mammalian embryos.

*Bulut HE et al; Okajimas Folia Anat Jpn 76 (1): 47-53*

Hazardous Substances Data Bank (HSDB)

The cytosine analog 5-azacytidine (5-AzaC) is a demethylating agent that is also known to induce mutagenesis in mammalian cells. In this study, the mutagenic potential of this drug was tested in the G10 and G12 transgenic Chinese hamster cell lines, which have a single bacterial gpt gene integrated into the genome at different sites, with its expression driven by a simian virus 40 (SV40) promoter. We show that the mutation frequencies following a 48-h exposure to different concentrations of 5-AzaC were 10 to 20 times higher than those of any of the other numerous mutagens that have been tested in the G10-G12 system. Moreover, the mutation frequencies were much higher in the G10 cell line than in the G12 cells. Detailed molecular analysis of the 6-thioguanine (6-TG)-resistant variants demonstrated that transgene silencing by de novo DNA methylation and increased chromatin condensation in the SV40 promoter was the major factor responsible for this high level of 6-TG resistance. As would be expected, exposure to 5-AzaC lowered the overall genomic DNA methylation levels, but it unexpectedly caused hypermethylation and increased chromatin condensation of the transgene in both the G10 and G12 cell lines. These results provide the first evidence that 5-AzaC may also induce transgene-specific DNA methylation, a phenomenon that can further be used for the elucidation of the mechanism that controls silencing of foreign DNA.

*Broday L et al; Mol Cell Biol 19 (4): 3198-204*

Hazardous Substances Data Bank (HSDB)

Retroviral sequence can silence transgene expression in vitro and in vivo. We report that this effect can be efficiently prevented by in vivo administration of the demethylating agent 5-azacytidine (aza-C). We engineered the U937 human cell line with a retroviral vector consisting of the thymidine kinase suicide gene (tk), which induces sensitivity to ganciclovir (gcv) and through an IRES sequence, the bacterial beta-galactosidase gene (lacZ) as a marker gene. About 90% of the U937 cells expressed the transgene. By injecting the transduced U937 cells in severe combined immunodeficient disease (SCID) mice, we generated a tumor which, during in vivo treatment with aza-C, maintained the high expression of lacZ and tk genes at the baseline values. LacZ-positive cells in the tumour masses after death was weak (1-2%) in the control group, while in mice treated with aza-C it was maintained at 90%. The delay in tumour onset was significantly longer when animals were treated with both aza-C and gcv ($P < 0.0001$) compared with animals treated with gcv or with aza-C alone. The prevention of silencing phenomena has important implications for gene therapy, because an efficient transduction associated with appropriate drug therapy, might be a powerful strategy for successful application of gene therapy protocols.

PMID:10476232

*Di Ianni M et al; Gene Ther 6 (4): 703-7 (1999)*

Hazardous Substances Data Bank (HSDB)

For more Non-Human Toxicity Excerpts (Complete) data for AZACITIDINE (10 total), please visit the HSDB record page.

Hazardous Substances Data Bank (HSDB)

### 13.1.11 Non-Human Toxicity Values

LD50 Mouse oral 572 mg/kg

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 295*

Hazardous Substances Data Bank (HSDB)

LD50 Mouse iv 229 mg/kg

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 295*

Hazardous Substances Data Bank (HSDB)

LD50 Mouse ip 68 mg/kg

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 295*

Hazardous Substances Data Bank (HSDB)

LD50 Dog iv 7200 ug/kg

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 295*

Hazardous Substances Data Bank (HSDB)

LD50 Wild bird oral 100 mg/kg

*Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996., p. 295*

Hazardous Substances Data Bank (HSDB)

### 13.1.12 Ongoing Test Status

The following link will take the user to the National Toxicology Program (NTP) Test Agent Search Results page, which tabulates all of the "Standard Toxicology & Carcinogenesis Studies", "Developmental Studies", and "Genetic Toxicity Studies" performed with this chemical. Clicking on the "Testing Status" link will take the user to the status (i.e., in review, in progress, in preparation, on test, completed, etc.) and results of all the studies that the NTP has done on this chemical. [http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=320-67-2]

*Available from: **https://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchresults&searchterm=320-67-2***

Hazardous Substances Data Bank (HSDB)

## 14 Associated Disorders and Diseases

- Comparative Toxicogenomics Database (CTD)

## 15 Literature

### 15.1 Coronavirus Studies

PubChem

### 15.2 NLM Curated PubMed Citations

PubChem

### 15.3 Springer Nature References

Springer Nature

### 15.4 Depositor Provided PubMed Citations

PubChem

## 15.5 Synthesis References

Lorenzo DE FERRA, Maurizio ZENONI, Stefano TURCHETTA, Mauro ANIBALDI, Ettore AMMIRATI, Paolo BRANDI, Giorgio BERARDI, "PROCESS FOR THE SYNTHESIS OF AZACITIDINE AND DECITABINE." U.S. Patent US20110245485, issued October 06, 2011.

DrugBank

## 15.6 Metabolite References

Human Metabolome Database (HMDB)

## 15.7 General References


1. Cihak A: Biological effects of 5-azacytidine in eukaryotes. Oncology. 1974;30(5):405-22. [PMID:4142650]
2. Kaminskas E, Farrell AT, Wang YC, Sridhara R, Pazdur R: FDA drug approval summary: azacitidine (5-azacytidine, Vidaza) for injectable suspension. Oncologist. 2005 Mar;10(3):176-82. [PMID:15793220]
3. Leone G, Voso MT, Teofili L, Lubbert M: Inhibitors of DNA methylation in the treatment of hematological malignancies and MDS. Clin Immunol. 2003 Oct;109(1):89-102. [PMID:14585280]
4. Ghoshal K, Bai S: DNA methyltransferases as targets for cancer therapy. Drugs Today (Barc). 2007 Jun;43(6):395-422. [PMID:17612710]
5. Silverman LR, Demakos EP, Peterson BL, Kornblith AB, Holland JC, Odchimar-Reissig R, Stone RM, Nelson D, Powell BL, DeCastro CM, Ellerton J, Larson RA, Schiffer CA, Holland JF: Randomized controlled trial of azacitidine in patients with the myelodysplastic syndrome: a study of the cancer and leukemia group B. J Clin Oncol. 2002 May 15;20(10):2429-40. [PMID:12011120]
6. Silverman LR: Targeting hypomethylation of DNA to achieve cellular differentiation in myelodysplastic syndromes (MDS). Oncologist. 2001;6 Suppl 5:8-14. [PMID:11700387]
7. Issa JP, Kantarjian H: Azacitidine. Nat Rev Drug Discov. 2005 May;Suppl:S6-7. [PMID:15962522]
8. O'Dwyer K, Maslak P: Azacitidine and the beginnings of therapeutic epigenetic modulation. Expert Opin Pharmacother. 2008 Aug;9(11):1981-6. doi: 10.1517/14656566.9.11.1981 . [PMID:18627335]
9. Siddiqui MA, Scott LJ: Azacitidine: in myelodysplastic syndromes. Drugs. 2005;65(13):1781-9; discussion 1790-1. [PMID:16114977]
10. Abdulhaq H, Rossetti JM: The role of azacitidine in the treatment of myelodysplastic syndromes. Expert Opin Investig Drugs. 2007 Dec;16(12):1967-75. [PMID:18042004]
11. Keating GM: Azacitidine: a review of its use in higher-risk myelodysplastic syndromes/acute myeloid leukaemia. Drugs. 2009;69(17):2501-18. doi: 10.2165/11202840-000000000-00000. [PMID:19911860]
12. Sullivan M, Hahn K, Kolesar JM: Azacitidine: a novel agent for myelodysplastic syndromes. Am J Health Syst Pharm. 2005 Aug 1;62(15):1567-73. [PMID:16030365]
13. Dapp MJ, Clouser CL, Patterson S, Mansky LM: 5-Azacytidine can induce lethal mutagenesis in human immunodeficiency virus type 1. J Virol. 2009 Nov;83(22):11950-8. doi: 10.1128/JVI.01406-09. Epub 2009 Sep 2. [PMID:19726509]
14. FDA Approved Drug Products: VIDAZA (azacitidine) injection
15. FDA Approved Drug Products: ONUREG (azacitidine) tablets
16. Health Canada Product Monograph: VIDAZA (azacitidine) injection


DrugBank

Kim et al. Permissive epigenomes endow reprogramming competence to transcriptional regulators. Nature Chemical Biology, doi: 10.1038/s41589-020-0618-6, published online 17 August 2020

Nature Chemical Biology

## 15.8 Chemical Co-Occurrences in Literature

PubChem

## 15.9 Chemical-Gene Co-Occurrences in Literature

PubChem

## 15.10 Chemical-Disease Co-Occurrences in Literature

PubChem

## 16 Patents

US8846628

DrugBank

### 16.1 Depositor-Supplied Patent Identifiers

PubChem

Link to all deposited patent identifiers

PubChem

### 16.2 WIPO PATENTSCOPE

Patents are available for this chemical structure:

https://patentscope.wipo.int/search/en/result.jsf?inchikey=NMUSYJAQQFHJEW-KVTDHHQDSA-N

PATENTSCOPE (WIPO)

### 16.3 FDA Orange Book Patents

| | |
|---|---|
| **Patent** | 8846628 |
| **Expiration** | Jun 3, 2030 |
| **Applicant** | CELGENE CORP |
| **Drug Application** | N214120 (Prescription Drug: ONUREG, Ingredients: AZACITIDINE) |

FDA Orange Book

# 17 Biomolecular Interactions and Pathways

## 17.1 Protein Bound 3D Structures

- RCSB Protein Data Bank (RCSB PDB)

View 1 protein in NCBI Structure

- PubChem

### 17.1.1 Ligands from Protein Bound 3D Structures

| | |
|---|---|
| PDBe Ligand Code | 5AE |
| PDBe Structure Code | 4QD3 |
| PDBe Conformer | |

- Protein Data Bank in Europe (PDBe)

## 17.2 Drug-Gene Interactions

- Drug Gene Interaction database (DGIdb)

## 17.3 Chemical-Gene Interactions

### 17.3.1 CTD Chemical-Gene Interactions

Comparative Toxicogenomics Database (CTD)

## 17.4 DrugBank Interactions

DrugBank

## 17.5 Drug-Drug Interactions

DrugBank

## 18 Biological Test Results

### 18.1 BioAssay Results

PubChem

## 19 Taxonomy

*The LOTUS Initiative for Open Natural Products Research: frozen dataset union wikidata (with metadata)* | **DOI:10.5281/zenodo.5794106**

- LOTUS - the natural products occurrence database

## 20 Classification

### 20.1 MeSH Tree

Medical Subject Headings (MeSH)

### 20.2 NCI Thesaurus Tree

NCI Thesaurus (NCIt)

### 20.3 ChEBI Ontology

ChEBI

### 20.4 KEGG: Drug

KEGG

## 20.5 KEGG: USP

KEGG

## 20.6 KEGG: ATC

KEGG

## 20.7 KEGG: Target-based Classification of Drugs

KEGG

## 20.8 WHO ATC Classification System

WHO Anatomical Therapeutic Chemical (ATC) Classification

## 20.9 FDA Pharm Classes

FDA Pharm Classes

## 20.10 ChemIDplus

ChemIDplus

## 20.11 CAMEO Chemicals

CAMEO Chemicals

## 20.12 ChEMBL Target Tree

ChEMBL

## 20.13 UN GHS Classification

UN Globally Harmonized System of Classification and Labelling of Chemicals (GHS)

## 20.14 NORMAN Suspect List Exchange Classification

- NORMAN Suspect List Exchange

## 20.15 EPA DSSTox Classification

- EPA DSSTox

## 20.16 International Agency for Research on Cancer (IARC) Classification

- International Agency for Research on Cancer (IARC)

## 20.17 LOTUS Tree

- LOTUS - the natural products occurrence database

## 20.18 FDA Drug Type and Pharmacologic Classification

- National Drug Code (NDC) Directory

## 21 Information Sources

FILTER BY SOURCE ALL SOURCES

1. **Burnham Center for Chemical Genomics**

   *SID56323580*
   *https://pubchem.ncbi.nlm.nih.gov/bioassay/1996#section=Data-Table*

2. **CAMEO Chemicals**

   LICENSE
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   https://cameochemicals.noaa.gov/help/reference/terms_and_conditions.htm?d_f=false

   *5-AZACYTIDINE*
   *https://cameochemicals.noaa.gov/chemical/19834*
   *CAMEO Chemical Reactivity Classification*
   *https://cameochemicals.noaa.gov/browse/react*

3. **DrugBank**

   LICENSE
   Creative Common's Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/legalcode)
   https://www.drugbank.ca/legal/terms_of_use

   *Azacitidine*
   *https://www.drugbank.ca/drugs/DB00928*

4. **Human Metabolome Database (HMDB)**

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   http://www.hmdb.ca/citing

   *Azacitidine*
   *http://www.hmdb.ca/metabolites/HMDB0015063*
   *HMDB0015063_nmr_one_2335*
   *https://hmdb.ca/metabolites/HMDB0015063#spectra*

5. **NCI Investigational Drugs**

   LICENSE
   https://www.cancer.gov/policies/copyright-reuse

   *AZACITIDINE*
   *http://dtp.nci.nih.gov/NCI-InvestigationalDrugsCI92/102816%20(1992).txt*

6. **CAS Common Chemistry**

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   *Azacytidine*
   *https://commonchemistry.cas.org/detail?cas_rn=320-67-2*

7. **ChemIDplus**

   LICENSE
   https://www.nlm.nih.gov/copyright.html

   *Azacitidine [USAN:INN:BAN]*
   *https://chem.nlm.nih.gov/chemidplus/sid/0000320672*
   *ChemIDplus Chemical Information Classification*
   *https://chem.nlm.nih.gov/chemidplus/*

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   https://www.cancer.gov/policies/copyright-reuse

   *Azacitidine*
   *https://dtp.cancer.gov/dtpstandard/servlet/dwindex?searchtype=NSC&outputformat=html&searchlist=758186*

9. **EPA DSSTox**

   LICENSE
   https://www.epa.gov/privacy/privacy-act-laws-policies-and-resources

   *5-Azacytidine*
   *https://comptox.epa.gov/dashboard/DTXSID9020116*
   *CompTox Chemicals Dashboard Chemical Lists*
   *https://comptox.epa.gov/dashboard/chemical-lists/*

10. **European Chemicals Agency (ECHA)**

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*2-(β-D-ribofuranosyl)-4-amino-1,3,5-triazin-2-one*
https://echa.europa.eu/substance-information/-/substanceinfo/100.005.711

11. ## Hazardous Substances Data Bank (HSDB)

*AZACITIDINE*
https://pubchem.ncbi.nlm.nih.gov/source/hsdb/6879

12. ## ChEBI

*5-azacytidine*
http://www.ebi.ac.uk/chebi/searchId.do?chebiId=CHEBI:2038

*ChEBI Ontology*
http://www.ebi.ac.uk/chebi/userManualForward.do#ChEBI%20Ontology

13. ## FDA Pharm Classes

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https://www.fda.gov/about-fda/about-website/website-policies#linking

*AZACITIDINE*
https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm

*FDA Pharmacological Classification*
https://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm162549.htm

14. ## LiverTox

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https://www.nlm.nih.gov/copyright.html

*Azacitidine*
https://www.ncbi.nlm.nih.gov/books/n/livertox/Azacitidine/

15. ## LOTUS - the natural products occurrence database

LICENSE

The code for LOTUS is released under the GNU General Public License v3.0.

https://lotus.nprod.net/

*LOTUS Tree*
https://lotus.naturalproducts.net/

16. ## NCI Thesaurus (NCIt)

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https://ncithesaurus.nci.nih.gov/ncitbrowser/ConceptReport.jsp?dictionary=NCI_Thesaurus&ns=ncit&code=C288

*NCI Thesaurus Tree*
https://ncit.nci.nih.gov

17. ## ClinicalTrials.gov

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18. ## Comparative Toxicogenomics Database (CTD)

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http://ctdbase.org/about/legal.jsp

https://ctdbase.org/detail.go?type=chem&acc=D001374

19. ## DailyMed

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*AZACITIDINE*
https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=AZACITIDINE

20. ## Drug Gene Interaction database (DGIdb)

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The data used in DGIdb is all open access and where possible made available as raw data dumps in the downloads section.

http://www.dgidb.org/downloads

https://www.dgidb.org/drugs/AZACITIDINE

21. ## Drug Induced Liver Injury Rank (DILIrank) Dataset

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https://www.fda.gov/about-fda/about-website/website-policies#linking

*azacitidine*
https://www.fda.gov/science-research/liver-toxicity-knowledge-base-ltkb/drug-induced-liver-injury-rank-dilirank-dataset

22. ## Nature Chemical Biology

https://pubchem.ncbi.nlm.nih.gov/substance/406176301

23. ## European Medicines Agency (EMA)

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*Azacitidine Mylan (EMEA/H/C/004984)*
*https://www.ema.europa.eu/en/medicines/human/EPAR/azacitidine-mylan*

*Azacitidine betapharm (EMEA/H/C/005075)*
*https://www.ema.europa.eu/en/medicines/human/EPAR/azacitidine-betapharm*

*Azacitidine Accord (EMEA/H/C/005147)*
*https://www.ema.europa.eu/en/medicines/human/EPAR/azacitidine-accord*

*Azacitidine Celgene (EMEA/H/C/005300)*
*https://www.ema.europa.eu/en/medicines/human/EPAR/azacitidine-celgene*

*Vidaza (EMEA/H/C/000978)*
*https://www.ema.europa.eu/en/medicines/human/EPAR/vidaza*

*azacitidine (P/0217/2015)*
*https://www.ema.europa.eu/en/medicines/human/paediatric-investigation-plans/emea-001272-pip02-13-m01*

*Onureg (EMEA/H/C/004761)*
*https://www.ema.europa.eu/en/medicines/human/EPAR/onureg*

24. ## NCI Cancer Drugs



*azacitidine*
*https://www.cancer.gov/about-cancer/treatment/drugs/azacitidine*

25. ## Drugs and Lactation Database (LactMed)



*Azacitidine*
*https://www.ncbi.nlm.nih.gov/books/NBK500962/*

26. ## EU Clinical Trials Register
*https://www.clinicaltrialsregister.eu/*

27. ## FDA Orange Book



*https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book*

28. ## NORMAN Suspect List Exchange



*NORMAN Suspect List Exchange Classification*
*https://www.norman-network.com/nds/SLE/*

29. ## WHO Anatomical Therapeutic Chemical (ATC) Classification



*https://www.whocc.no/atc/*

*ATC Code*
*https://www.whocc.no/atc_ddd_index/*

30. ## National Drug Code (NDC) Directory



*AZACITIDINE*
*https://www.fda.gov/drugs/drug-approvals-and-databases/national-drug-code-directory*

31. ## FDA/SPL Indexing Data



*M801H13NRU*
*https://www.fda.gov/ForIndustry/DataStandards/SubstanceRegistrationSystem-UniqueIngredientIdentifierUNII/*

32. ## SpectraBase

*5-Azacytidine*
*https://spectrabase.com/spectrum/7t1erV9xnLy*

*5-Azacytidine*
*https://spectrabase.com/spectrum/KuzghW9gKFX*

*5-Azacytidine*
*https://spectrabase.com/spectrum/H6Gcjcqa1uv*

*5-Azacytidine*
*https://spectrabase.com/spectrum/JTudjAlUHud*

*5-Azacytidine*
*https://spectrabase.com/spectrum/8SntjqXhiJQ*

33. International Agency for Research on Cancer (IARC)



*Azacitidine*
*https://monographs.iarc.who.int/list-of-classifications*

*IARC Classification*
*https://www.iarc.fr/*

34. NIPH Clinical Trials Search of Japan
*https://rctportal.niph.go.jp/en/*

35. NITE-CMC

*5-Azacytidine - FY2007*
*https://www.nite.go.jp/chem/english/ghs/07-mhlw-0076e.html*

36. NLM RxNorm Terminology



*https://rxnav.nlm.nih.gov/id/rxnorm/1251*

37. NMRShiftDB
*https://pubchem.ncbi.nlm.nih.gov/substance/114918057*

38. Protein Data Bank in Europe (PDBe)
*http://www.ebi.ac.uk/pdbe-srv/pdbechem/chemicalCompound/show/5AE*

39. PubChem
*https://pubchem.ncbi.nlm.nih.gov*

40. RCSB Protein Data Bank (RCSB PDB)



*https://www.rcsb.org/*

41. Springer Nature
*https://pubchem.ncbi.nlm.nih.gov/substance/341141221*

42. Wikidata



*Azacitidine*
*https://www.wikidata.org/wiki/Q416451*

43. Medical Subject Headings (MeSH)



*Azacitidine*
*https://www.ncbi.nlm.nih.gov/mesh/68001374*

*MeSH Tree*
*http://www.nlm.nih.gov/mesh/meshhome.html*

*Enzyme Inhibitors*
*https://www.ncbi.nlm.nih.gov/mesh/68004791*

*Antimetabolites, Antineoplastic*
*https://www.ncbi.nlm.nih.gov/mesh/68000964*

44. KEGG



*Therapeutic category of drugs in Japan*
*http://www.genome.jp/kegg-bin/get_htext?br08301.keg*

*USP drug classification*
*http://www.genome.jp/kegg-bin/get_htext?br08302.keg*

*Anatomical Therapeutic Chemical (ATC) classification*
*http://www.genome.jp/kegg-bin/get_htext?br08303.keg*

*Target-based classification of drugs*
*http://www.genome.jp/kegg-bin/get_htext?br08310.keg*

45. UN Globally Harmonized System of Classification and Labelling of Chemicals (GHS)

*GHS Classification Tree*
*http://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.html*

46. ChEMBL

*ChEMBL Protein Target Tree*
*https://www.ebi.ac.uk/chembl/g/#browse/targets*

47. **PATENTSCOPE (WIPO)**
*SID 388556103*
*https://pubchem.ncbi.nlm.nih.gov/substance/388556103*

48. **NCBI**
*https://www.ncbi.nlm.nih.gov/projects/linkout*