3. Silvani A, *et al.* Intra-arterial ACNU and carboplatin versus intravenous chemotherapy with cisplatin and BCNU in newly diagnosed patients with glioblastoma. *Neurol Sci* 2002; **23:** 219–24.
4. Weller M, *et al.* Neuro-Oncology Working Group 01 trial of nimustine plus teniposide versus nimustine plus cytarabine chemotherapy in addition to involved-field radiotherapy in the first-line treatment of malignant glioma. *J Clin Oncol* 2003; **21:** 3276–84.
5. Watanabe T, *et al.* Human interferon beta, nimustine hydrochloride, and radiation therapy in the treatment of newly diagnosed malignant astrocytomas. *J Neurooncol* 2005; **72:** 57–62.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: ACNU; ***Jpn:*** Nidran†; ***Neth.:*** ACNU†; ***Switz.:*** ACNU†.

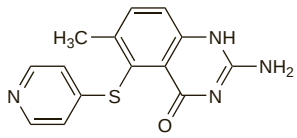
Nolatrexed *(rINN)*

AG-337 (nolatrexed dihydrochloride); Nolatrexedum. 2-Amino-6-methyl-5-(4-pyridylthio)-4(3*H*)-quinazolinone.

Нолатрексед

$C_{14}H_{12}N_4OS$ = 284.3.

CAS — 147149-76-6 (nolatrexed); 152946-68-4 (nolatrexed dihydrochloride).



Profile

Nolatrexed is, like raltitrexed (p.766), a selective inhibitor of thymidylate synthase. It has been investigated as an antimetabolite antineoplastic for the treatment of hepatocellular carcinoma, although results of single-agent studies have been disappointing. It is also under investigation in combination therapy for other solid tumours.

◊ References.

1. Mok TS, *et al.* A multi-centre randomized phase II study of nolatrexed versus doxorubicin in treatment of Chinese patients with advanced hepatocellular carcinoma. *Cancer Chemother Pharmacol* 1999; **44:** 307–11.
2. Hughes AN, *et al.* Clinical pharmacokinetic and in vitro combination studies of nolatrexed dihydrochloride (AG337, Thymitaq) and paclitaxel. *Br J Cancer* 2000; **82:** 1519–27.
3. Estlin EJ, *et al.* A phase I study of nolatrexed dihydrochloride in children with advanced cancer. *Br J Cancer* 2001; **84:** 11–18.
4. Pivot X, *et al.* Result of two randomized trials comparing nolatrexed (Thymitaq) versus methotrexate in patients with recurrent head and neck cancer. *Ann Oncol* 2001; **12:** 1595–9.
5. Jhawer M, *et al.* Phase II trial of nolatrexed dihydrochloride [Thymitaq, AG 337] in patients with advanced hepatocellular carcinoma. *Invest New Drugs* 2007; **25:** 85–94.
6. Gish RG, *et al.* Phase III randomized controlled trial comparing the survival of patients with unresectable hepatocellular carcinoma treated with nolatrexed or doxorubicin. *J Clin Oncol* 2007; **25:** 3069–75.

Oblimersen Sodium *(USAN, rINNM)*

G-3139; Natrii Oblimersenum; Oblimersén sódico; Oblimersen Sodique.

Натрий Облимерсен

$C_{172}H_{204}N_{62}Na_{17}O_{91}P_{17}S_{17}$ = 6058.3.

CAS — 190977-41-4.

Profile

Oblimersen sodium is an antisense oligonucleotide that blocks the production of BCL-2, a mitochondrial protein that prevents apoptosis. It is under investigation for the treatment of various malignant neoplasms, including leukaemias, lung cancer, and malignant melanoma.

◊ References.

1. Frankel SR. Oblimersen sodium (G3139 Bcl-2 antisense oligonucleotide) therapy in Waldenstrom's macroglobulinemia: a targeted approach to enhance apoptosis. *Semin Oncol* 2003; **30:** 300–304.
2. Büchele T. Proapoptotische Therapie mit Oblimersen (bcl-2-Antisense-Oligonukleotid)—Übersicht über präklinische und klinische Daten. *Onkologie* 2003; **26** (suppl 7): 60–9.
3. Herbst RS, Frankel SR. Oblimersen sodium (Genasense bcl-2 antisense oligonucleotide): a rational therapeutic to enhance apoptosis in therapy of lung cancer. *Clin Cancer Res* 2004; **10** (suppl): 4245s–4248s.
4. Chi KN. Targeting Bcl-2 with oblimersen for patients with hormone refractory prostate cancer. *World J Urol* 2005; **23:** 33–7.
5. O'Brien SM, *et al.* Phase I to II multicenter study of oblimersen sodium, a Bcl-2 antisense oligonucleotide, in patients with advanced chronic lymphocytic leukemia. *J Clin Oncol* 2005; **23:** 7697–7702.
6. Mita MM, *et al.* A phase I, pharmacokinetic and biologic correlative study of oblimersen sodium (Genasense, G3139) and irinotecan in patients with metastatic colorectal cancer. *Ann Oncol* 2006; **17:** 313–21.
7. Bedikian AY, *et al.* Bcl-2 antisense (oblimersen sodium) plus dacarbazine in patients with advanced melanoma: the Oblimersen Melanoma Study Group. *J Clin Oncol* 2006; **24:** 4738–45.
8. O'Brien S, *et al.* Randomized phase III trial of fludarabine plus cyclophosphamide with or without oblimersen sodium (Bcl-2 antisense) in patients with relapsed or refractory chronic lymphocytic leukemia. *J Clin Oncol* 2007; **25:** 1114–20. Correction. *ibid.* 2008; **26:** 820.

Ofatumumab *(rINN)*

HuMax-CD20; Ofatumumabum. Immunoglobulin G1, anti-(human CD20 (antigen))(human monoclonal HuMax-CD20 heavy chain), disulfide with human monoclonal HuMax-CD20 κ-chain, dimer.

Офатумумаб

CAS — 679818-59-8.

Profile

Ofatumumab is an anti-CD20 monoclonal antibody that is under investigation for the treatment of non-Hodgkin's lymphoma and chronic lymphocytic leukaemia.

◊ References.

1. Coiffier B, *et al.* Safety and efficacy of ofatumumab, a fully human monoclonal anti-CD20 antibody, in patients with relapsed or refractory B-cell chronic lymphocytic leukemia: a phase 1-2 study. *Blood* 2008; **111:** 1094–1100.
2. Hagenbeek A, *et al.* First clinical use of ofatumumab, a novel fully human anti-CD20 monoclonal antibody in relapsed or refractory follicular lymphoma: results of a phase 1/2 trial. *Blood* 2008; **111:** 5486–95.
3. Robak T. Ofatumumab, a human monoclonal antibody for lymphoid malignancies and autoimmune disorders. *Curr Opin Mol Ther* 2008; **10:** 294–309.

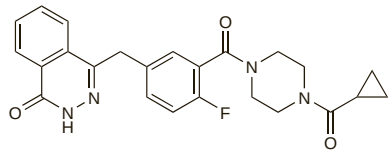
Olaparib *(rINN)*

Olaparibum. 4-[(3-{[4-(Cyclopropylcarbonyl)piperazin-1-yl]carbonyl}-4-fluorophenyl)methyl]phthalazin-1(2*H*)-one.

Олапариб

$C_{24}H_{23}FN_4O_3$ = 434.5.

CAS — 763113-22-0.



Profile

Olaparib is an antineoplastic that is under investigation for the treatment of ovarian cancer.

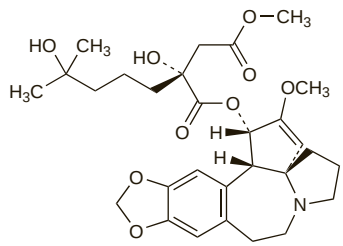
Omacetaxine Mepesuccinate *(pINN)*

CGX-635; HHT; Homoharringtonine; Mepesuccinato de omacetaxina; NSC-141633; Omacétaxine, Mépésuccinate d'; Omacetaxini mepesuccinas. 1-[(1*S*,3a*R*,14b*S*)-2-Methoxy-1,5,6,8,9,14b-hexahydro-4*H*-cyclopenta[*a*][1,3]dioxolo[4,5-*h*]pyrrolo[2,1-*b*][3]benzazepin-1-yl] 4-methyl (2*R*)-2-hydroxy-2-(4-hydroxy-4-methylpentyl)butanedioate.

Омацетаксин Мепесукцинат

$C_{29}H_{39}NO_9$ = 545.6.

CAS — 26833-87-4.



Pharmacopoeias. In *Chin.*

Profile

Omacetaxine mepesuccinate is a semisynthetic formulation of homoharringtonine, which is an alkaloid derived from the tree *Cephalotaxus harringtonia*, and related species. It is thought to induce apoptosis by inhibition of protein synthesis. It is under investigation for the treatment of chronic myeloid leukaemia (p.653). It has also been tried in the treatment of acute leukaemias and other neoplastic disorders.

The related compounds harringtonine, isoharringtonine, and deoxyharringtonine have also been investigated.

Adverse effects of omacetaxine mepesuccinate may include severe hypotension, cardiac arrhythmias, myelosuppression, gastrointestinal disturbances, chest pain, headache, fatigue, alopecia, rashes, and hyperglycaemia.

◊ References.

1. Kantarjian HM, *et al.* Homoharringtonine and low-dose cytarabine in the management of late chronic-phase chronic myelogenous leukemia. *J Clin Oncol* 2000; **18:** 3513–21.
2. Kantarjian HM, *et al.* Homoharringtonine: history, current research, and future direction. *Cancer* 2001; **92:** 1591–1605.
3. O'Brien S, *et al.* Simultaneous homoharringtonine and interferon-alpha in the treatment of patients with chronic-phase chronic myelogenous leukemia. *Cancer* 2002; **94:** 2024–32.
4. Tang J, *et al.* A homoharringtonine-based regimen for childhood acute myelogenous leukemia. *Med Pediatr Oncol* 2003; **41:** 70–2.
5. O'Brien S, *et al.* Results of triple therapy with interferon-alpha, cytarabine, and homoharringtonine, and the impact of adding imatinib to the treatment sequence in patients with Philadelphia chromosome-positive chronic myelogenous leukemia in early chronic phase. *Cancer* 2003; **98:** 888–93.
6. Luo CY, *et al.* Homoharringtonine: a new treatment option for myeloid leukemia. *Hematology* 2004; **9:** 259–70.
7. Quintás-Cardama A, Cortes J. Homoharringtonine for the treatment of chronic myelogenous leukemia. *Expert Opin Pharmacother* 2008; **9:** 1029–37.
8. Quintás-Cardama A, Cortes J. Omacetaxine mepesuccinate - a semisynthetic formulation of the natural antitumoral alkaloid homoharringtonine, for chronic myelocytic leukemia and other myeloid malignancies. *IDrugs* 2008; **11:** 356–72.

Oregovomab *(USAN, rINN)*

MAb-B43.13; Orégovomab; Oregovomabum. Immunoglobulin G1, anti-(human CA125 (carbohydrate antigen)) (mouse monoclonal B43.13 γ1-chain), disulfide with mouse monoclonal B43.13 κ-chain, dimer.

Ореговомаб

CAS — 213327-37-8.

Profile

Oregovomab is a murine monoclonal antibody that binds to CA-125, an antigen that is overexpressed in the majority of ovarian cancer patients, and stimulates an immune response to the tumour cells. It is under investigation for the treatment of ovarian cancer.

Oxaliplatin *(BAN, USAN, rINN)*

JM-83; NSC-266046; *l*-OHP; Oksaliplatiini; Oksaliplatin; Oksaliplatina; Oxaliplatina; Oxaliplatine; Oxaliplatino; Oxaliplatinum; RP-54780; SR-96669. [(1*R*,2*R*)-1,2-Cyclohexanediamine-*N*,*N*′]-[oxalato(2-)-*O*,*O*′]platinum.

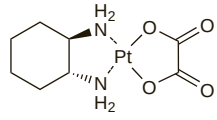
Оксалиплатин

$C_8H_{14}N_2O_4Pt$ = 397.3.

CAS — 61825-94-3.

ATC — L01XA03.

ATC Vet — QL01XA03.



Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Oxaliplatin). A white or almost white, crystalline powder. Slightly soluble in water; practically insoluble in dehydrated alcohol; very slightly soluble in methyl alcohol.

Incompatibility. Licensed product information states that oxaliplatin should not be mixed with chloride-containing solutions (including sodium chloride) or alkaline drugs or solutions. In particular, oxaliplatin should not be mixed with fluorouracil or any trometamol salts. While oxaliplatin may be infused through a Y-site with folinic acid (in glucose 5% solution), they may not be mixed in the same infusion bag, and folinic acid must not contain trometamol as an excipient. The infusion line should be flushed with glucose 5% before giving any other medication. Oxaliplatin may degrade on contact with aluminium, and injection equipment containing aluminium should not be used.

Stability. UK licensed product information states that oxaliplatin must be diluted in glucose 5% to give a concentration not less than 200 micrograms/mL. From a microbiological point of view, the infusion preparation should be used immediately; the infusion should not be stored for longer than 24 hours at 2° to 8° unless it has been prepared in controlled and validated aseptic conditions. Chemical and physical stability has been shown for 48 hours at 2° to 8°, and for 24 hours at 25°. US licensed product information states that, after dilution in 250 to 500 mL of glucose