



STN is operated in North America  
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## STN Database Summary Sheet

**ADISINSIGHT (Adis R&D Insight)** contains the full text of reports, i.e., profiles, on drugs in active research and development by the international pharmaceutical industry. New drugs are added to the database when they appear in the earliest laboratory report and are followed through to world market launch. Every scientific or commercial development of the drug's progress to market is assessed, evaluated, and reported. Adis editors check all the information to ensure the integrity and timeliness of the information.

The records in this file contain generic names, synonyms, trade names, CAS Registry Numbers<sup>®</sup>, EphMRA ATC codes, WHO ATC codes, developing companies, development stages by indication and country, licensed forecast information from Lehman Brothers, and Adis's own unique therapeutic value rating. The text includes an introduction, evaluation, commercial summary, clinical overview, adverse effects, pharmacology with pharmacokinetics and pharmacodynamics, and therapeutic trials. Bibliographic references are also included.

### Subject Coverage

- Weekly reports on new drugs in research, changes in development phases, and licensing availability

### Sources

- Direct contact with companies involved with research and development
- 1,700 biomedical and medical journals
- International meetings and conferences
- Company annual reports
- News services
- Press releases
- Licensed Lehman Brothers' PharmaPipelines data

### File Data

- 1998 to the present
- More than 20,245 records (11/05)
- Updated weekly
- Automatic current-awareness searches (SDIs) are run weekly

### User Aids

- Online helps (HELP DIRECTORY lists all available help messages)
- STNGUIDE

### Database Producer

Adis International Limited  
Chowley Oak Lane  
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Nakai Building  
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E-mail: helpdesk@jaici.or.jp (Technical Service)  
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**ADISINSIGHT****Search and Display Field Codes**

The field that allows left truncation (/CNS) is marked with an asterisk.

Search Field Name	Search Code	Search Examples	Display Codes
Basic Index (contains single words from the classification code (CC), development status (DSTA), evaluation (EVAL), text (TX), revision note (RNTE), company name (CO), chemical name (CN), controlled term (CT), and geographic term (GT) fields, as well as molecular formulas (MF) and CAS Registry Numbers (RN))	None (or /BI)	S IMMUNOSTIMULANTS S ANTI-ATHER? S GLAXO (L) ORIGINATOR S MECHANISM(L)IMMUNOMODULATORS S C (1W) GO S VACCINE# (P) USE S C10H10N2O5 S 47931-85-1	CC, CN, CO, DSTA, EVAL, MF, RN, RNTE, TX
Accession Number Change Date (1)	/AN /CDAT	S 1998:9493/AN S CDAT>19980100 S JULY 2, 1998/CDAT	AN CDAT
Chemical Name (includes chemical names, generic names, synonyms, and trade names)	/CN	S POLOXAMER 188 NF/CN	CN
Chemical Name Segment*	/CNS	S (METHYL (L) THIAZOL)/CNS S ?AMINO BUTYRYL?/CNS S (SALBUTAMOL AND SCHERING)/CNS	CN
Classification Code (EphMRA ATC codes and WHO ATC codes) (code and text) (2)	/CC	S R03/CC S R3/CC S "ANTI-ACNE PREPARATIONS"/CC S TOPICAL PREPARATIONS/CC	CC
Company Name (2) (corporate name and location)	/CO	S SMITHKLINE UNITED KINGDOM/CO S LICENSEE (L) INTROGEN/CO	CO
Controlled Term (indication)	/CT	S ALZHEIMER?/CT S ANXIETY DISORDERS/CT	DSTA
Development Status (development phase, location, and indication)	/DSTA	S (PHASE II (L) GERMANY)/DSTA S (STROKE (L) PRECLINICAL)/DSTA	DSTA
Document Number	/DN	S 002345/DN	DN
Element Count, Specific (1)	/Element symbol	S 1/N AND 3/O	MF
Entry Date (1)	/ED	S L1 AND ED>=19990700	Not displayed
Evaluation	/EVAL	S (DIABETES AND TYPE AND 1)/EVAL	EVAL
Evaluation Score (1)	/EVAL.S	S DIABETES/EVAL (L) EVAL.S>=80	EVAL
Field Availability (code and text)	/FA	S EVALUATION/FA S L1 AND RN/FA	FA
Geographic Term (code and text)	/GT	S GERMANY/GT S DE/GT	DSTA
Highest Development Phase	/HDP	S PHASE III/HDP	HDP
Journal Title	/JT	S ADIS R&D INSIGHT/JT	JT, SO
Molecular Formula	/MF	S C10H10N2O5/MF S C18 H22 N2 O S . CI H/MF	MF
Number of Components (1)	/NC	S L6 AND NC>=2	MF
Other Source (Adis Alerts Accession Number)	/OS	S "800007351"/OS	OS
Periodic Group	/PG	S T3/PG	MF
Reference	/RE	S JOURNAL OF PHARMACOLOGY/RE	RE
Revision Date (1)	/RDAT	S 19980312/RDAT	RDAT
Revision Note	/RNTE	S PRECLINICAL DEV?/RNTE	RNTE
Source	/SO	S ADIS R&D INSIGHT/SO	SO
Trade Name	/TN	S TANADOPA/TN	CN
Update Date (1)	/UP	S L1 AND UP>=19990600	Not displayed
Word Count (1)	/WC	S L1 AND WC	WC

## DISPLAY and PRINT Formats

Any combination of formats may be used to display or print answers. Multiple codes must be separated by spaces or commas, e.g., D L1 1-5 CN EVAL. The fields are displayed or printed in the order requested.

Hit-term highlighting is available for all fields except FA, STF, STR, and STS. Highlighting must be ON during SEARCH in order to use the HIT, KWIC, and OCC formats.

Format	Content	Examples
AN CC CDAT (1) CN CO DN DSTA EVAL (2) FA (2) HDP JT (2) MF OS RDAT (RNTE) RE RN SO STF STR (3) STS (2,3) TN (2) TX WC	Accession Number Classification Code (EphMRA ATC codes and WHO ATC codes) Change Date Chemical Name (Generic Names, Synonyms, Chemical Name, and Trade Names) (includes TN) Company Name (corporate name and location) (Originator, Parent, Licensee, and Other) Document Number Development Status (development status, location, and indication) Evaluation (indication, score, and route) Field Availability Highest Development Phase Journal Title Molecular Formula Other Source (Adis Alerts Accession Number) Revision Date and Revision Note Reference CAS Registry Number and Related CAS Registry Number Source Flat Structure (no stereo indicated) Structure Diagram (includes stereo bonds and R/S/E/Z labels when available) Stereo Structure (includes stereo bonds when available) Trade Name Text (Introduction, Evaluation, Commercial Summary (table with Company, Major Markets, Launch Date, Commercial Value, and Patent Expiry), Pharmacology Overview (Mechanism of action, Route of Elimination), Clinical Overview, Adverse Events, Pharmacology (Pharmacokinetics, Clinical Studies), and Therapeutic Trials) (includes EVAL) Word Count	D AN D 1-3 CC D CDAT D CN STR D CO 1,3-5 D AN DN D DSTA D EVAL D FA D HDP D JT 2 D CN MF D OS D RDAT D RE L1 4 D RN 3,4 D SO D L9 1 3 D L4 STR D STS D TN D TX D WC
ALL (3) DALL (3) IALL (3) IDE (3) IIDE (3) ISTD (3) SCAN (1,4) STD (3) TRIAL (1) (SAM, TRI)	AN, SO, DN, CDAT, CN, MF, RN, STR, related RN, CC, HDP, DSTA, CO, OS, WC, TX, RDAT, RNTE, RE ALL, delimited for post-processing ALL, indented with text labels AN, SO, DN, CDAT, CN, MF, RN, STR, related RN, CC, HDP, CO, OS, WC IDE, indented with text labels (IIDE is the default) STD, indented with text labels CN (Generic Name) (random display, no answer number) AN, SO, DN, CDAT, CN, MF, RN, STR, related RN, CC, HDP, DSTA, CO, OS, WC, TX CN (Generic Name), CDAT	D ALL D DALL D IALL D IDE D L2 3 IIDE D D ISTD D SCAN D STD D TRIAL TOTAL
HIT KWIC OCC (1)	Fields containing hit terms Hit terms with 20 words on either side (KeyWord-In-Context) Number of occurrences of hit terms and fields in which they occur	D HIT D KWIC NOH D OCC

(1) No online display fee for this format.

(2) Custom display format only.

(3) Stereo structure diagrams are available only on graphics terminals and offline prints.

(4) SCAN must be entered on the command line, i.e., DISPLAY SCAN, D SCAN.

## ADISINSIGHT

### SELECT, ANALYZE, and SORT Fields

The SELECT command is used to create E-numbers containing terms taken from the specified field in an answer set.

The ANALYZE command is used to create an L-number containing terms taken from the specified field in an answer set.

The SORT command is used to rearrange the search results in either alphabetic or numeric order of the specified field(s).

Field Name	Field Code	ANALYZE/ SELECT (1)	SORT
Accession Number	AN	Y	N
CAS Registry Number	RN	Y (2)	N
CAS Registry Number and Chemical Name	CHEM	Y (3)	N
Change Date	CDAT	Y	Y
Chemical Name	CN	Y (4) (default)	N
	NAME	Y (5)	N
Classification Code (EphMRA and WHO ATC codes)	CC	Y	Y
Company Name (Corporation Name)	CO	Y	Y
Controlled Term (Indication)	CT	Y (6)	N
Development Status	DSTA	Y	N
Document Number	DN	Y	Y
Evaluation	EVAL	Y	N
Geographic Term	GT	Y (6)	N
Highest Development Phase	HDP	Y	Y
Journal Title	JT	Y	Y
Molecular Formula	MF	Y	Y
Occurrence Count of Hit Terms	OCC	N	Y
Other Source (Adis Alerts Accession Number)	OS	Y (7)	Y
Reference	RE	Y	N
Revision Date	RDAT	Y (6)	N
Revision Note	RNTE	Y (6)	N
Source	SO	Y	N
Text	TX	Y (8)	N
Trade Name	TN	Y	N
Word Count	WC	N	Y

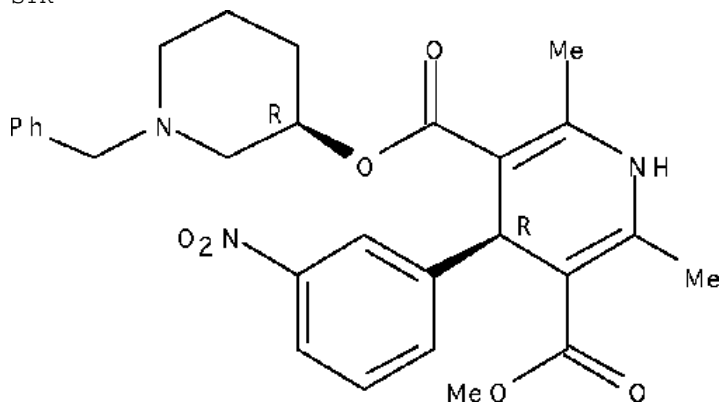
- (1) HIT may be used to restrict terms extracted to terms that match the search expression used to create the answer set, e.g., SEL HIT CN.
- (2) Selects or analyzes the CAS Registry for the substance and the related CAS Registry Numbers with /BI appended to the terms created by SELECT.
- (3) Selects or analyzes the CAS Registry for the substance, the related CAS Registry Numbers, Generic Names, Synonyms, Chemical Name, and Trade Names) with /BI appended to the terms created by SELECT.
- (4) Selects or analyzes the Generic Names, Synonyms, Chemical Name, and Trade Names).
- (5) Selects or analyzes the Generic Names, Synonyms, Chemical Name, and Trade Names with /BI appended to the terms created by SELECT.
- (6) SELECT HIT and ANALYZE HIT are not valid with this field.
- (7) Appends /DN to the terms created by SELECT.
- (8) Appends /BI to the terms created by SELECT.

## Full-Text Browsing

User Request	Example	System Response
DISPLAY BROWSE	=> DISPLAY BROWSE ENTER (L1) OR L#: ENTER (DIS), ANSWER NUMBERS, OR END:	NOVICE version
D BRO  Answer number(s)  Answer number(s) and format Format only  Change default format  Forward n fields Backward n fields Search forward for character string Search backward for character string End DISPLAY BROWSE	=> D BRO L1 : :1-3  :4 HIT :TI TX  :*KWIC  :F3 :B1 :S BONE MARROW  :S -NAUSEA  :END =>	EXPERT version  display answers 1, 2, and 3 in default format display answer 4 in HIT format display title and text of last answer displayed change default to KWIC no answer displayed move forward 3 fields move backward 1 field search forward within record for 'bone marrow' search backward within record for 'nausea' exit DISPLAY BROWSE and return to => prompt

**ADISINSIGHT****Sample Records****DISPLAY ALL**

AN 1998:1 ADISINSIGHT  
 SO Adis R&D Insight  
 DN 000001  
 CDAT Jun 30, 1998  
 CN Benidipine  
 CN KW 3049; Nakadipine  
 CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl 1-(phenylmethyl)-3-piperadiny l ester, (R\*,R\*)-(+)-  
 CN Coniel  
 MF C28 H31 N3 O6  
 RN 105979-17-7  
 STR



RN 91599-74-5  
 CC EPHMRA ATC CODE: C8A Calcium Antagonists, Plain  
 CC WHO ATC CODE: C08C-A Dihydropyridine derivatives  
 HDP Launched  
 DSTA Launched, Japan, Angina pectoris  
 Launched, Japan, Essential hypertension  
 Phase III, Italy, Angina pectoris  
 Phase III, Italy, Essential hypertension  
 Phase II, Germany, Angina pectoris  
 Phase II, United States, Angina pectoris  
 Phase II, United Kingdom, Angina pectoris  
 Phase II, Germany, Essential hypertension  
 Phase II, United States, Essential hypertension  
 Phase II, United Kingdom, Essential hypertension  
 ORIGINATOR: Kyowa Hakko (Japan)  
 PARENT: Kyowa Hakko  
 LICENSEE: Crinos  
 OTHER: Ranbaxy Laboratories  
 OS 800375302; 800498965; 800193530  
 WC 649

**TX TEXT****Introduction:**

Benidipine (nakadipine, KW 3049) is a calcium antagonist. It is being developed by Kyowa Hakko for the treatment of essential hypertension and angina pectoris. It has been launched in Japan (as Coniel sup((R,)), has been approved in India, and is undergoing phase III clinical trials in Italy and phase II trials in Germany, the United Kingdom and the USA. Benidipine is licensed to Crinos.

**DISPLAY ALL (cont'd)**

TX EVALUATION:  
Hypertension 80 (PO).

TX COMMERCIAL SUMMARY:  
Hypertension/angina / Ca antagonist

Company	Region	Launch Date	Peak Sales	Patent Expiry
KYOWA HAKKO	Jap	1991	\$244m	n/a

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TX PHARMACOLOGY OVERVIEW:  
Pharmacodynamics:  
Coronary and cerebral vasodilatory effects in vivo; marked BP-lowering effects; diuresis; natriuresis

Mechanism of action:  
Calcium channel antagonists  
Ion channel antagonists

TX CLINICAL OVERVIEW:  
Route(s) of Administration: PO  
Adverse events:  
rare: Diarrhoea, Oedema.

TX Adverse Events:  
In 55 patients with essential hypertension receiving benidipine 2-8 mg/day for <= 1 year, adverse events included lightheadedness (n = 1), diarrhoea (1) and peripheral oedema (1)/1/.

TX PHARMACOLOGY:  
Pharmacodynamics (Hypertension):  
Preclinical studies: the long term effects of ceronapril 40 mg/kg/day, AE 0047 20 mg/kg/day and benidipine 10 or 20 mg/kg/day were examined in stroke-prone spontaneously hypertensive rats. In treated rats, the incidence of cerebrovascular lesions was significantly depressed and their life-spans were extended compared to the untreated control rats. AE 0047 sustained BP under 210mm Hg without developing fibrinoid deposition on arterial walls. After benidipine, thickened arterial walls were observed and BP remained over 250mm Hg. In contrast to benidipine, ceronapril reduced the occurrence of smooth muscle proliferation and BP levels were similar to those of benidipine/2/.

Clinical studies: in an open Japanese study in 7 patients and 5 volunteers, benidipine lowered BP significantly, increased urinary volume and urinary sodium excretion, and significantly reduced the pressor response to angiotensin II and norepinephrine. The antihypertensive effects of benidipine may be related to a direct vasodilatory effect, as well as to natriuresis, diuresis and a blunting of the pressor actions of angiotensinamide and norepinephrine.

A randomised, single-blind, crossover study in 15 salt-sensitive patients with essential hypertension assessed the efficacy of benidipine and controlled release nifedipine on sodium-induced changes in systemic and regional haemodynamics. Oral benidipine 4-8 mg/day once daily for 73 days significantly reduced MAP and increased CI, superior mesenteric blood flow and renal blood flow during low and high sodium intake. Nifedipine 10-30 mg/day also significantly reduced MAP during low sodium intake, but had no effects on HR, CI or regional blood flow. The high sodium diet increased MAP, CI and terminal aortic flow (all p < 0.05), and reduced mesenteric and renal blood flows (p < 0.05) during nifedipine administration/3/.

In 15 patients with essential hypertension, benidipine 4 mg/day and trandolapril 1 mg/day for 12 weeks similarly decreased BP, and increased

**ADISINSIGHT****DISPLAY ALL (cont'd)**

concentrations of nitrite/nitrate (NOx) and cGMP. Neither agent affected HR, lipid profiles and renal functions/4/.

In 10 elderly patients with essential hypertension undergoing mental arithmetic test, administration of oral benidipine 4mg od for 12 weeks significantly decreased 24-h BP, and had no marked effect on HR. However, the decrease in night-time DBP was not significant, and the decrease in night-time SBP was minimal. In benidipine recipients, the increase in SBP induced by mental arithmetic test was significantly decreased compared with baseline/5/.

Pharmacodynamics (Ischaemic Heart Disease):

Benidipine suppresses ischaemic ECG changes and attenuates ST and T wave elevation in animal models. Mild and long lasting dose-dependent increases in coronary sinus outflow and decreases in BP are seen at doses > 1 microg/kg IV. Benidipine protects the ischaemic canine myocardium and maintains global cardiohaemodynamics. Other animal studies have shown that benidipine exhibits preferential coronary and cerebral vasodilating activity, and has a longer duration of action than nifedipine or nicardipine.

**TX THERAPEUTIC TRIALS:**

Hypertension:

In patients with essential hypertension (n = 21), oral once daily benidipine 4 mg/day for 2 weeks produced a long lasting reduction in BP compared with baseline/6/.

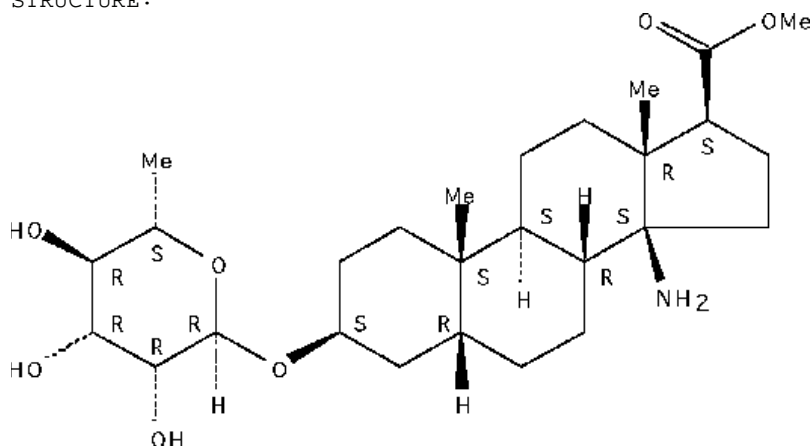
In an open, multicentre study in 78 patients with essential hypertension, monotherapy with oral benidipine 2-8 mg/day od for <= 1 year significantly decreased BP from baseline. Similar effect was achieved when benidipine was used in combination with other antihypertensive agents (n = 19) (details not provided). 42% of patients in the benidipine monotherapy group and 44% of patients in the combination therapy group had their BP normalised at 1 year (BP < 150/90mm Hg)/1/.

RDAT	RNTE
05 Jul 1999	Registered for Angina pectoris in India (PO)
05 Jul 1999	Registered for Essential hypertension in India (PO)
30 Apr 1999	A study has been added to the Hypertension pharmacodynamics field (746001)
06 Apr 1999	Sales forecasts reviewed by Lehman Brothers
29 Sep 1998	A study has been added to the Hypertension pharmacodynamics field (691650)
11 Nov 1994	A preclinical study has been added to the hypertension pharmacodynamics field (307950)

- RE
1. Imazu M, Yamabe T, et al. Antihypertensive effects and safety of long-term treatment with benidipine hydrochloride in essential hypertensive patients. *Shinryo to Shinyaku*. 32: 995-1005, 1995. (Japanese). 800375302
  2. Ohta Y, Chikugo T, et al. Long term therapeutic effects of ACE inhibitor and calcium antagonists on hypertensive vascular lesions in M-SHRSP. *Clinical and Experimental Pharmacology and Physiology*. (Suppl. 1): 103, 1994. (English).
  3. Shimamoto H, Shimamoto Y. Benidipine counteracts sodium-induced alterations in systemic and regional hemodynamics. *Blood Pressure*. 6: 18-23, Jan 1997. (English). 800498965
  4. Takase H, Sugiyama M, et al. Effect of antihypertensive therapy with benidipine or trandolapril on serum nitrite/nitrate levels in essential hypertension. *Journal of Hypertension*. 16 (Suppl. 2): 99, Jun 1998. (English).
  5. Muneta S, Kohara K, et al. Effects of benidipine hydrochloride on 24-hour blood pressure and blood pressure response to mental stress in elderly patients with essential hypertension. *International Journal of Clinical Pharmacology and Therapeutics*. 37: 141-147, Mar 1999. (English).
  6. Nakanishi T, Takahashi H, et al. Effects of benidipine hydrochloride on 24-hour blood pressure. *Current Therapeutic Research*. 53: 270-276, Mar 1993. (English). 800193530

## DISPLAY IIIDE

ACCESSION NUMBER: 1998:1107 ADISINSIGHT  
SOURCE: Adis R&D Insight  
DOCUMENT NO: 001241  
CHANGE DATE: Aug 10, 1998  
GENERIC NAME: LND 796  
SYNONYM: LNF 209  
CHEMICAL NAME: Androstane-17-carboxylic acid,  
14-amino-3-((6-dexoxy-alpha-L-  
mannopyranosyl)oxy)-, methyl ester, (3beta, 5beta,  
14beta, 17beta)-  
TRADE NAME: Cordil  
MOLECULAR FORMULA: C27 H45 N O7  
CAS REGISTRY NO.: 118549-42-1  
STRUCTURE:



RELATED CAS REG. NO.: 122322-73-0  
EPHMRA ATC CODE: C1A1 Plain cardiac glycosides  
WHO ATC CODE: C01A Cardiac Glycosides  
HIGHEST DEV. PHASE: No Development Reported

## COMPANY INFORMATION

ORIGINATOR: Nativelle (France)  
PARENT: Procter & Gamble  
OTHER: Procter & Gamble; Rohm

OTHER SOURCES: 800165260  
WORD COUNT: 260