

Adis R&D Insight

FILE DESCRIPTION

Adis R&D Insight comprehensively reports on the latest developments of drugs in active research and development internationally each week. More than 25,000 drugs are included in the database. Drugs reported in Adis R&D Insight start with the earliest laboratory report and continue through to world market launch. Every scientific or commercial development advancing the drug's progress to market is assessed, evaluated, and reported in Adis R&D Insight.

Adis R&D Insight is compiled from information collected from many sources. The primary sources are: direct contact with companies involved with research and development, information collected from drug and therapeutic literature published in more than 2,300 medical and biomedical journals, attendance at international meetings and conferences, company annual reports, news services, press releases, and licensed Lehman Brothers' PharmaPipelines data.

Adis editors check all the information before reporting in R&D Insight to ensure the integrity and timeliness of the published information.

File 107 is the public file; File 907 is the subscriber file, available to those who subscribe to a qualifying Wolters Kluwer Pharma Solutions product.

SUBJECT COVERAGE

Information reported in **Adis R&D Insight** includes: generic name, synonyms, brand names, developing companies, development phases by indication and country, adverse events, pharmacology, pharmacokinetics, pharmacodynamics, therapeutic trials, development history, licensed forecast information from Lehman Brothers, and Adis's own unique therapeutic value rating. Adis R&D Insight profiles are also backed by more than 10,000 evaluated Adis scientific summaries and 63,000 bibliographic references.

TIPS

USE FILE 107

to find R&D information on drug research from laboratory discovery to launch.

USE MAP

to extract CAS® Registry Numbers for searching in other pharmaceutical databases:

MAP RN TEMP

EXPAND ON DP=

to choose a developmental phase:

EXPAND DP=PHASE III

ENTER HELP CODES 107

to see WHO ATC and EphMRA ATC codes.

ENTER HELP EVAL 107

to find definitions of Adis Evaluation.

DIALOG FILE DATA

Inclusive Dates: 1986 to present

Update Frequency: Weekly

File Size:

25,000+ records as of December 2009 (File 107)

and 25,000+ records as of December 2009 (File 907)

CONTACT

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SAMPLE RECORD

DIALOG(R)File 107:Adis R&D Insight
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AA= 00244846 014306
/NA,NA= Drug Name: Ezetimibe/simvastatin
/TN,TN=
RD= Record Revision Date: 20050323

/NA,NA= Brand Name: Inegy(TM); Vytorin(TM); Zintrepid(TM)

/NA,NA= Synonyms: Simvastatin/ezetimibe; Zetia(TM)/Zocor sup((R)); Zocor sup((R))/ Zetia(TM)
/SY,SY=

/NA,NA= Chemical Name: 1-(4-Fluorophenyl)-3(R)-(3(S)-(4-fluorophenyl)-3- hydroxypropyl)-4(S)-
/CN,CN= (4-hydroxyphenyl)azetid-2-one compd. with Butanoic acid, 2,2-dimethyl-, 1,2,3,7,8,8a-hexahydro-3,7- dimethyl-8-(2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl)-1- naphthalenyl ester, (1S-(1alpha,3alpha,7beta,8beta(2S*,-4S*),8abeta))-

MF= Molecular Formula: C49H59F2N08
DR=,RN= Related CAS® Registry Number: 163222-33-1; 163380-16-3 ((3R-(3alpha(R*),4beta))- isomer); 79902-63-9

AC= WHO ATC Code: C10A - Cholesterol and Triglyceride Reducers; C10A-A01 - Simvastatin
CC= EPHMRA ATC Code: C10 - Hypolipidaemics/Anti-Atheroma Preparations; C10A - Cholesterol and Triglyceride Reduction Preparations; C10A1 - HMG CoA reductase inhibitors
ME= Mechanism of Action: HMG-CoA reductase inhibitors; Reductase inhibitors; Oxidoreductase inhibitors; Enzyme inhibitors; Cholesterol absorption inhibitors

/CO,CO= Originator Company: Merck/Schering-Plough Pharmaceuticals (USA)
/LO,LO=
/CO,CO= Parent Company: Merck & Co - Schering-Plough (JV)
/IP,IP=

DP= Highest Phase: Launched

/ST,ST= Development Status: Launched, Germany, Hypercholesterolaemia
 Launched, Mexico, Hypercholesterolaemia
 Launched, USA, Hypercholesterolaemia
 Registered, European Union, Hypercholesterolaemia
 Preregistration, New Zealand , Hypercholesterolaemia
 Phase III, USA, Acute coronary syndromes

/TX,IT Text:
 Introduction:
 Schering-Plough and Merck & Co. have formed a joint venture, Merck/Schering-Plough Pharmaceuticals, to develop and market ezetimibe and simvastatin as a once-daily fixed-combination tablet (Vytorin(TM), Zintrepid(TM), Inegy(TM)). It is proposed that the combination tablet will be developed for all four doses of simvastatin (10-40mg). Ezetimibe is a cholesterol-absorption inhibitor, whereas simvastatin decreases endogenous liver production of cholesterol by inhibiting HMG-CoA reductase. Combination of these two different cholesterol-lowering mechanisms could achieve additive or synergistic cholesterol-lowering effects. In September 2001, Merck Sharp & Dohme in Singapore opened a manufacturing facility and the plant manufactures the ezetimibe/simvastatin fixed dose tablets.
 (...)

/CS,TX Commercial Summary: High cholesterol levels / Cholesterol absorption inhibitor

 Company Region Launch Date Peak Sales Patent Expiry

 Merck US 2004 \$2800m
 Merck ex-US 2004 \$1000m
 Schering Plough US 2004 \$2800m
 Schering Plough ex-US 2004 \$1000m

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/EV,SC=,EV= ADIS Evaluation:
 Hypercholesterolaemia 72 (PO).

SAMPLE RECORD (cont'd)

/TX,PO=	<p>Pharmacology Overview:</p> <p>Pharmacodynamics: Immunogenicity: Mechanism of action: HMG-CoA reductase inhibitors Reductase inhibitors Oxidoreductase inhibitors Enzyme inhibitors Cholesterol absorption inhibitors Activity versus parent drug: unspecified parent</p>
/TX,CV	<p>Clinical Overview: Route(s) of Administration: PO Administration Freq.(per day): Adverse events: rare: Elevated aminotransferase levels, Hepatitis, Musculoskeletal pain, Pancreatitis, Rhabdomyolysis, Thrombocytopenia. Drug Interactions: Unknown. No interaction between ezetimibe and simvastatin in volunteers with LDL cholesterol levels > 130 mg/dl</p>
/TX/AE	<p>Adverse Events: Comparative studies: ezetimibe/simvastatin was well tolerated with an overall safety profile similar to atorvastatin monotherapy among 788 patients with hypercholesterolaemia in a 24-week, randomised, placebo- controlled, phase III study. There were no clinically or statistically significant differences in the incidence of muscle enzyme elevations or consecutive liver (...) Drug Interactions: Ezetimibe did not affect the pharmacokinetics of simvastatin in a placebo-controlled phase I study. In this trial, volunteers with LDL cholesterol levels > 130 mg/dl (n = 58) were randomised to receive treatment PO od dl-14 with simvastatin 10mg with or without ezetimibe 0.25, 1 or 10mg. There were no significant differences in C sub(max), AUC and CL/F between treatment groups/11/. Pharmacokinetics: Pharmacodynamics (Hyperlipidaemia): In a study, 24 volunteers with LDL cholesterol levels > 130 mg/dL were randomised to receive ezetimibe 10mg, simvastatin 20mg, or a combination of the two, for 14 days. The coadministration of ezetimibe and simvastatin was well tolerated and decreased LDL-cholesterol and total cholesterol, compared with simvastatin or ezetimibe alone/12/.</p>
/TX/TR	<p>Therapeutic Trials: Hyperlipidaemia: The efficacy and safety of ezetimibe and simvastatin co-administration was assessed in 100 patients with heterozygous familial hypercholesterolaemia, coronary heart disease, or multiple cardiovascular risk factors. While on simvastatin 20 mg/day, patients were randomised to (...)</p>
/UP,UP=	<p>Drug Update Information: 10-Feb-2003: A clinical study has been added to the Hyperlipidaemia pharmacodynamics section (924160) 14-Dec-2001: Investigation in Hypercholesterolaemia in USA (PO) 13-Dec-2001: Financial Figures have been added 04-Dec-2001: Sales forecasts reviewed by Lehman Brothers 26-Jul-2000: Investigation in Hypercholesterolaemia in USA (PO) 26-Jul-2000: New profile</p>
/CR,CR=	<p>References: 1. Merck/Schering-Plough Pharmaceuticals. Merck/Schering-Plough Pharmaceuticals Announces Submission of Application to FDA for Ezetimibe/Simvastatin Tablet, an Investigational Cholesterol-Lowering Medicine Release. : 17 Nov 2003. Available from: URL: http://www.merck.com. (English). 2. Schering-Plough Corporation. Schering-Plough Reports Financial Results for 2003 Fourth Quarter, Full (...)</p>
XR=	<p>References No.: 800974093; 800974092; 800974094; 809041635; 800823732; 800934101; 809041121</p>

BASIC INDEX

SEARCH SUFFIX	DISPLAY CODE	FIELD NAME	INDEXING	SELECT EXAMPLES
—	—	All Basic Index Fields	Word	S GERMANY
/AE	AE	Adverse Effects Text ¹	Word	S ADVERSE(W)EVENT?/AE
/CN	CN	Chemical Name ²	Word	S HYDROXYPHENYL(W)AZETIDIN/CN
/CO	CO	Company Name ^{2,3}	Word	S MERCK(W)SCHERING/CO
/CR	CR	References ²	Word	S ANNOUNCE?(W)SUBMISSION?/CR
/CS	CS	Commercial Summary ¹	Word	S CHOLESTEROL(W)ABSORPTION/CS
/CV	CV	Clinical Overview ¹	Word	S MUSCULOSKELETAL(W)PAIN/CV
/EV	EV	Adis Evaluation ^{2,4}	Word	S HYPERCHOLESTEROLAEMIA(S)72/EV
/IP	IP	Parent Company Name ²	Word	S MERCK/IP
/IT	IT	Introductory Text ¹	Word	S CHOLESTEROL(W)LOWERING/IT
/LI	LI	Licensee ²	Word	S ASTRA/LI
/LO	LO	Originator Company Name ²	Word	S MERCK(W)SCHERING/LO
/NA	NA	Drug Name ^{2,5}	Word & Phrase	S EZETIMIBE/NA S 'ZETIMIBE/SIMVASTATIN'/NA
/PC	PC	Pharmacology Text ¹	Word	S RESISTANT(W)ENTEROCOCCI/PC
/PO	PO	Pharmacology Overview ¹	Word	S REDUCTASE(W)INHIBITOR?/PO
/RR	RR	Related CAS Registry Numbers	Phrase	S 163222-33-1/RR
/ST	ST	Development Status ²	Word	S BACTERIAL(W)INFECTIONS/ST
/SY	SY	Synonyms ²	Word & Phrase	S ZETIA/SY S ZOCOR SUP?/SY
/TN	TN	Brand Name ²	Word	S INEGY/TN
/TR	TR	Therapeutic Trial Text ¹	Word	S CORONARY(W)HEART/TR
/TX	TX	Text ⁶	Word	S LIVER(W)PRODUCTION/TX
/UP	UP	Drug Update Information ²	Word	S CLINICAL(W)STUDY/UP

¹ Also searchable and displayable with TX.

² Searchable in the Basic Index and in the Additional Indexes.

³ Includes Originator, Parent Company, Other Companies, and Licensee.

⁴ Enter HELP EVAL 107 to see descriptions online.

⁵ Includes Brand Name, Chemical Name, and Synonyms.

⁶ /TX includes: AE, CS, CV, IT, PC, PO, TR.

ADDITIONAL INDEXES

SEARCH PREFIX	DISPLAY CODE	FIELD NAME	INDEXING	SELECT EXAMPLES
AA=	AA	IP Accession Number	Phrase	S AA=004877
AC=	AC	WHO ATC Codes and Descriptions ⁷	Word & Phrase	S AC=(TRIGLYCERIDE(W)REDUCER) S AC='CHOLESTEROL AND TRIGLYCERIDE'?
AM=	PO	Active Metabolites	Phrase	S AM=NO
—	AN	DIALOG Accession Number		
CC=	CC	EphMRA ATC Codes and Descriptions ⁷	Word & Phrase	S CC=(REDUCTASE(W)INHIBITORS) S CC=C10A1
CC=	CC	EphMRA ATC Codes and Descriptions ⁷	Phrase	S CC='HYPOLIPIDAEMICS/ANTI-ATHEROMA'?
CN=	CN	Chemical Name ^{2,11}	Phrase	S CN=1-(4-FLUOROPHENYL)?
CO=	CO	Company Name ^{2,3}	Phrase	S CO=MERCK & CO?
CR=	CR	References ²	Word	S CR=(ANNOUNCE?(W)SUBMISSION?)
DP=	DP	Highest Phase of Development	Word & Phrase	S DP=LAUNCHED S DP=PHASE III
DR=	DR	Drug of Record CAS Number ⁸	Phrase	S DR=163222-33-1
EL=	PO	Route of Elimination	Phrase	S EL=RENAL?
EV=	EV	Adis Evaluation ^{2,4}	Phrase	S EV=HYPERCHOLESTROLAEMIA(S)72
IP=	IP	Parent Company Name ²	Phrase	S IP=MERCK & CO - SCHERING?
LI=	LI	Licensee ²	Phrase	S LI=ASTRA?
LK=	PO	Linear Kinetics	Phrase	S LK=YES
LO=	LO	Originator Company Name ²	Phrase	S LO='MERCK/SCHERING'?
ME=	ME	Mechanism of Action	Word & Phrase	S ME=(REDUCTASE(W)INHIBITORS) S ME=CHOLESTEROL ABSORPTION?
MF=	MF	Molecular Formula	Phrase	S MF=C49H59F2NO8
NA=	NA	Drug Name ^{2,5}	Phrase	S NA=ZINTREPID(TM)
RD=	RD	Record Revision Date ^{9,10}	Phrase	S RD=20050323
RN=	RN	CAS(R) Registry Number ¹²	Phrase	S RN=79902-63-9
SC=	SC	Adis Rating of Therapeutic Value	Numeric	S SC>=70(S)EV=HYPERCHOLESTEROLAEMIA
ST=	ST	Development Status ²	Phrase	S ST=PREREGISTRATION NEW ZEALAND?
SY=	SY	Synonyms ^{2,11}	Phrase	S SY=ZETIA(TM)?
TN=	TN	Brand Name ^{2,11}	Phrase	S TN=INEGY(TM)
UD=	—	Update	Phrase	S UD=9999
UP=	UP	Drug Update Information ²	Word	S UP=(FINANCIAL(W)FIGURES)
XR=	XR	Reference Number	Phrase	S XR=800974093

⁷ Codes are assigned by Adis. Enter HELP CODES 107 to view codes online.

⁸ Also is searchable as RN=

⁹ Revision Date is changed only when there are significant changes in the content of the record.

¹⁰ Also searchable as PD=

¹¹ Also searchable as NA=

¹² Includes drug of record CAS Registry Number and Related CAS Registry Number.

SPECIAL FEATURES

For command descriptions, enter HELP SORT, HELP RANK, HELP MAP online.

SORT	AC, CC, CO, LO, ME, NA, RD, SC	SORT S2/ALL/CC SORT S3/ALL/SC
RANK	All phrase- and numeric-indexed fields in the Additional Indexes can be ranked.	RANK CO S3
MAP	LO, NA, RN, SY, SYRN, XR	MAP NA TEMP S2 MAP SYRN TEMP S1

PREDEFINED FORMAT OPTIONS

NO.	DIALOGWEB FORMAT	RECORD CONTENT
1	--	DIALOG Accession Number
2	--	Drug Name, Synonyms, Brand Name, Chemical Name, Originator Company, Parent Company, Licensee, Other Company, Highest Phase, WHO ATC Codes, EphMRA ATC Codes, and Record Revision Date
3	Medium	Development Status, Adis Evaluation, Commercial Summary, Clinical Overview, Pharmacology Overview, Mechanism of Action, Introduction Text, and all information provided in Format 2
4	--	Full Record with Tagged Fields
5	--	Full Record
6	Free	Drug Name and Record Revision Date
7	Long	Full Record except CAS Registry Number, Related CAS Registry Number, Molecular Formula, References, and Reference Numbers
8	Short	Drug Name and Record Revision Date
9	Full	Full Record
K	--	KWIC (Key Word In Context) displays a window of text; may be used alone or with other formats

OTHER OUTPUT OPTIONS

For an explanation, enter HELP TYPE, HELP UDF, HELP TAG online.

USER DEFINED FORMATS	User-defined formats can be specified using the display codes indicated in the Search Options tables.	TYPE S3/NA,AE,RR/1-5 PRINT S2/NA,SY,SC/ALL
TAG	TAG can be used for tagged fields.	TYPE S1/9/ALL TAG PRINT S3/5/1-10 TAG DISPLAY S2/2/ALL TAG
DIRECT RECORD ACCESS	DIALOG Accession Number	TYPE 00123456/9 DISPLAY 00238215/5 PRINT 00654321/4

FOR ONLINE HELP:

See HELP FIELDS 107 for searchable fields; HELP FORMAT 107 for output formats; HELP LIMIT 107 for limits; HELP RATES 107 for cost information; HELP SORT 107 for sorts.