Adis R&D Insight

Description

Adis R&D Insight provides international coverage of drugs in research and development. Drugs are monitored through all development phases and information includes: an Adis evaluated rating of therapeutic value, adverse events, pharmacology, pharmacokinetics, pharmacodynamics, pharmacoeconomics, therapeutic trials, and development phases by indication and country.

Data is collected from more than 2,300 biomedical journals covering drugs and therapeutics, news services, newsletters, company annual reports, contact with companies, market intelligence, meetings and conferences.

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
- Adis's forecasts of Approval Probability, and Revenue

Adis R&D Insight profiles are also backed by more than 10,000 evaluated Adis scientific summaries and 63,000 bibliographic references.

Date Coverage

1995–present

Update Frequency

Weekly

Geographic Coverage

International

Document Types

Reports

Publisher

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TI Sumatriptan needle-free injection

PUB,PD **Adis R&D Insight**. (Mar 19, 2013).

TX **Full text** Translate

DRUG PROFILE - Sumatriptan needle-free injection

Zogenix has developed a needle-free subcutaneous injection formulation of sumatriptan utilising its DoseProTM (formerly Intraject ®) technology for the treatment of acute migraines. Sumatriptan is a serotonin $_{1D}$ receptor agonist that is already available in tablet, nasal spray and autoinjection device formulations. Originally developed by Aradigm and later acquired by Zogenix, the needle-free injectable formulation of sumatriptan has been developed in an effort to address inconvenience and needle phobia issues with currently available injectable triptans. The product delivers sumatriptan 6mg in 0.5mL of sterile liquid. Sumavel ® DoseProTM has been launched in the US, making this product the first needle-free injectable triptan approved for the treatment of migraine and cluster headaches. The product has also been launched in selected countries in the EU, and Norway.

The DoseProTM (formerly Intraject ®) needle-free delivery uses a single-use, pen-sized system that delivers liquid drug formulations rapidly and comfortably to the subcutaneous (SC) layers of the skin. The technology comprises two main components - a glass drug capsule with a prefilled volume of 0.5mL, and a compact nitrogen gas power source (actuator). Upon activation, the prefilled device creates a short-lived pressure peak in the skin, allowing the drug to be delivered comfortably to the intended region. The entire delivery is completed in <60 milliseconds. Following application, the local tissues absorb the drug, enabling entry into the systemic circulation.

Zogenix is evaluating a number of potential pharmaceutical partners who have expressed interest in promoting sumatriptan DoseProTM (Reference: 809132467).

COMPANY AGREEMENTS

Mallinckrodt LLC entered into a co-promotion agreement with Zogenix in June 2012 for sumatriptan needle-free injection. Under terms of the agreement, Mallinckrodt will market the product in the US, and will be compensated by Zogenix based on a percentage of net sales. Focused co-promotion under the agreement was initiated in October 2012. The agreement runs to the end of June 2014, and may be extended in 6-month increments (Reference: 809147460) (Reference: 809138114) (Reference: 809138124).

In March 2012, the exclusive co-promotion and marketing agreement between Zogenix and Astellas Pharma US for sumatriptan DoseProTM, in the US, was terminated. The companies had entered into the agreement in August 2009. Under the agreement, Astellas was to focus primarily on marketing to primary care physicians and Zogenix was to focus on the neurology market. Astellas received payments based on sales performance within the specified target market. Upon termination, Zogenix assumed full responsibility for the continued commercialisation of sumatriptan DoseProTM, with a focus on headache specialists, neurologists and primary care physicians. Astellas contributed its agreed portion of marketing expenses through 31 March 2012, and continued to earn a product sales service fee during the period; Zogenix paid no further service fees to Astellas from the beginning of the second quarter of 2012 (Reference: 809147460) (Reference: 809132467) (Reference: 809132477) (Reference: 809103546).

Zogenix and Desitin Pharmaceuticals entered into a licensing agreement for sumatriptan DoseProTM in March 2008. Under the terms of the agreement, Desitin will receive exclusive rights for the formulation in the EU, and will be responsible for all development, commercialisation and marketing of sumatriptan DoseProTM in the EU. Zogenix will manufacture and supply the product and will receive royalty payments on future sales (Reference: 809086515).

In August 2006, Zogenix purchased the DoseProTM (formerly Intraject ®) subcutaneous delivery technology and related assets, including those related to sumatriptan needle-free injection, from Aradigm Corporation. Aradigm received an upfront payment of $US4 million and is eligible to receive additional milestone and royalty payments on sumatriptan needle-free injection and any future products based on the DoseProTM technology (Reference: 809073712). Following the US launch of sumatriptan needle-free injection in January 2010, Aradigm stated that it will receive quarterly royalty payments on sales (Reference: 809109213). Aradigm is entitled to 3% royalty on net sales of sumatriptan needle-free injection in all territories (Reference: 809120497). Aradigm received $US4 million milestone payment from Zogenix based on the first commercial sale in the US of Sumavel ® DoseProTM in February 2010 (Reference: 809122947).

KEY DEVELOPMENT MILESTONES

Sumavel ® DoseProTM was approved in Germany and the UK in January 2011. The Federal Institute for Drugs and Medical Devices of Germany (BrArM) and the Medicines and Healthcare products Regulatory Agency of the United Kingdom (MHRA) approved the MAA for sumatriptan injection for the acute treatment of migraine attacks, with or without aura, and the acute treatment of cluster headache (Reference: 809123730) (Reference: 809120560). In December 2010, sumatriptan needle-free injection was approved in Denmark for the same indication. Germany is the reference member state for the MAA under the EU decentralised procedure (Reference: 809120497) (Reference: 809119548). Desitin filed for approval in the EU in October 2009. The filing followed the completion of a European bioequivalence trial which compared Sumavel ® DoseProTM with Imigran ® injection (Reference: 809106298). The product has since been launched in Germany, Denmark, Sweden, the UK, Norway and France, with launches in other European countries to follow.

Zogenix and Astellas launched sumatriptan injection as Sumavel ® DoseProTM in the US in January 2010. The product was approved in the US in July 2009 for the treatment of migraine, with or without aura, and for the acute treatment of cluster headaches. Following submission of the NDA in December 2001, the company received a complete response letter from the US FDA in October 2008, citing the need for a single additional *in vitro* trial. Zogenix has also raised $US18 million in private placements to fund the commercialisation of the product (Reference: 809103546) (Reference: 809103023) (Reference: 809097956).

In April 2011, Zogenix established a Named Patient Programme for Sumavel ® DoseProTM enabling physicians to legally and ethically prescribe this agent in regions where the drug has not yet been approved. Clinigen Pharma, a UK-based global provider of specialist and unlicensed medicines, will manage the programme and supply the drug to healthcare providers (Reference: 809123730).

Zogenix has completed three trials in the US under its sumatriptan DoseProTM Pivotal Clinical Trial Program. The company reported that adverse events in the three trials were consistent with those previously observed with injectable sumatriptan, and included injection site reactions, tingling and warm sensations, dizziness and flushing.

Under the programme, a trial conducted in December 2007 investigated the effects of repeated injections of sumatriptan using the DoseProTM system to the same anatomical site (NCT00620425) (Reference: 700031945).

Results from the second phase II trial in the Pivotal Clinical Trial Programme were released by Zogenix in June 2008 (NCT00530517) (Reference: 700027377). The data showed that 98% of patients with migraine were able to use sumatriptan DoseProTM correctly during an acute migraine attack (Reference: 809090609).

Zogenix completed the first trial in the Pivotal Clinical Trial Programme in April 2007 (NCT00614029). The randomised, open-label cross-over pharmacokinetics and bioequivalence trial included 54 healthy subjects. Results revealed that sumatriptan administered via the DoseProTM system was bioequivalent to the needle-based Imitrex STATdose System ® after injection into the most commonly used injection sites such as the thigh and abdomen (Reference: 700030841).

Positive results from two pharmacokinetic studies of sumatriptan needle-free injection in healthy volunteers showed that sumatriptan administered via the DoseProTM system met all bioequivalence criteria and demonstrated equivalent pharmacokinetics to the marketed injectable product (Reference: 809042041) (Reference: 809051270) (Reference: 700190396) (Reference: 700190628).

Zogenix entered into a $US30 million royalty financing agreement with Cowen Healthcare Royalty Partners II in June 2011 (Reference: 809126756).

In July 2010, Zogenix secured a $US35 million loan. Additionally, Zogenix investors contributed an additional $US15 million. These funds will be partially used as working capital to fund commercial launch activities (Reference: 809114566).

Aradigm received a $US4 million milestone payment from Zogenix in February 2010. The milestone payment was triggered by the first commercial sale of sumatriptan needle-free injection in the US (Reference: 809109213).

In September 2009, Zogenix completed $US51 million in series B preferred stock financing. $US36 million has been closed, with the remaining $US15 million to be available between December 2009 and February 2010. Zogenix plans to use this to finance the launch of needle-free sumatriptan in the US (Reference: 809105118).

Zogenix arranged for a $US10 million loan from GE Healthcare Financial Services in March 2007. The resources were used to finance the launch of sumatriptan needle-free injection (Reference: 809073630).

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PATENT INFORMATION

Zogenix has a US patent (No. 7 776 007) for Sumavel ® DoseProTM needle-free delivery system, which expires in 2025 (Reference: 809122851).

Zogenix's US Patent No. 5 891 086 covers a particular activator mechanism forming a part of the needleless injector device, which expires in 2014. Corresponding patents in Canada, in Germany, Spain, France, UK, Italy and Japan, expire in 2013. US Patent No. 6 135 979 covers a needleless injector with particular safety mechanisms, and expires in 2017. Corresponding patents in Germany, France, UK and Japan expire in 2016. US Patent No. 5 957 886 claiming a needleless injector system using a viscous damping medium expires in 2016, with corresponding patents in Canada, Germany, France, UK and Japan expiring in 2015. US Patent No. 7 776 007 covering a cap and latch mechanism expires in 2026; a corresponding patent exists in Japan. US Patent No. 7 901 385 covering a casing for enclosing the injection device expires in 2026, with corresponding patents available in Australia, Canada, Germany, Spain, France, UK, Italy, and Japan. US. Patents 5 891 086, 6 135 979, 5 957 886, 7 776 007 and 7 901 385 are listed in the FDA Orange Book for Sumavel ® DoseProTM.

Pharmacokinetics

Results revealed that maximum plasma concentrations of sumatriptan were reached in approximately 12 minutes in healthy volunteers after administration of the drug as sumatriptan DoseProTM. Sumatriptan DoseProTM was bioequivalent to the needle-based autoinjector product IMITREX STATdose ® at injection sites in the thigh and abdomen but not the arm. The mean ratios of the two devices were between 90.1 and 115% (Reference: 801156287) (Reference: 809106153) (Reference: 809090609).
The pharmacokinetics of subcutaneously injected sumatriptan and sumatriptan administered with the DoseProTM device were found to be similar in a study in 18 volunteers (Reference: 809042041). Similar findings were obtained in another phase I study in 24 volunteers who self-administered sumatriptan using the DoseProTM device, demonstrating bioequivalent blood plasma concentrations of the drug to those seen in volunteers treated with a subcutaneous (SC) needle injection of sumatriptan (Reference: 809051270).

Therapeutic Trials

Advances in the Treatment of Nausea and Migraine

Sumatriptan administered through the needle-free injection system was self-administered successfully on the first attempt in 51/52 patients. This clinical study involved 52 outpatients treating migraine attacks with the primary endpoint being successful use of the needle-free system (Reference: 801156287) (Reference: 809106153).

PROBABILITY OF APPROVALS

Migraine, Probability: 100, Comparative grade: NYR

REVENUE FORECASTS (in USD millions)

Indication: Migraine
Year: 2007, USA: 0, Europe: 0, Japan: 0
Year: 2008, USA: 0, Europe: 0, Japan: 0
Year: 2009, USA: 0, Europe: 0, Japan: 0
Year: 2010, USA: 19, Europe: 0, Japan: 0
Year: 2011, USA: 25, Europe: 15, Japan: 2
Year: 2012, USA: 33, Europe: 20, Japan: 2
Year: 2013, USA: 43, Europe: 24, Japan: 3
Year: 2014, USA: 54, Europe: 34, Japan: 3
Year: 2015, USA: 60, Europe: 35, Japan: 4
Year: 2016, USA: 63, Europe: 36, Japan: 4
Year: 2017, USA: 65, Europe: 37, Japan: 4
Year: 2018, USA: 63, Europe: 38, Japan: 4

REF

References

801156287. Needle-free subcutaneous sumatriptan (Sumavel TM DosePro TM): bioequivalence and ease of use. Brandes JL, Cady RK, Freitag FG, Smith TR, Chandler P, Fox AW, Linn L, Farr SJ. Headache. 49: 1435-1444, No. 10, Nov-Dec 2009. Summary in 2 parts (Part A). English. USA

809042041. Aradigm Announces Results From Clinical Study of Intraject Needle-Free System With Sumatriptan. Aradigm Corporation. Media Release. : 17 Nov 2004. Available from: URL: http://www.aradigm.com. English. USA

809051270. Aradigm Advances Development of Intraject Sumatriptan With New Clinical Trial Data. Aradigm Corporation. Media Release. : 29 Jun 2005. Available from: URL: http://www.aradigm.com. English. USA

809073630. Zogenix Closes $10 Million Deal with GE Healthcare Financial Services. Zogenix. Media Release. : 20 Mar 2007. Available from: URL: http://www.zogenix.com. English. USA

809073712. Aradigm Announces Asset Sale of Intraject(r) Needle-free Technology. Aradigm Corporation. Media Release. : 28 Aug 2006. Available from: URL: http://www.zogenix.com. English. USA

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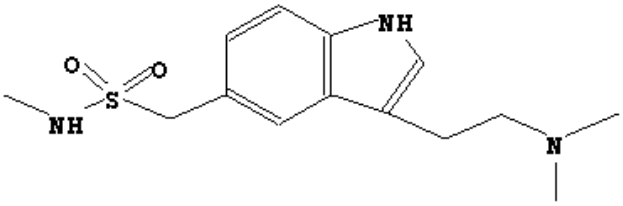

History of Drug Development

Event date	Update date	Update type	Significant	Details
20041117	20050928	Phase Change	false	Phase-I clinical trials in Migraine in USA (SC)
20050629	20050928	Scientific Update	true	Clinical data from a media release have been added to the pharmacokinetics section (9051270)
20050928	20050928	Phase Change	true	Phase-III clinical trials in Migraine in USA (SC)
20060828	20070322	Licensing Status	false	Zogenix acquires sumatriptan needle-free injectable from Aradigm Corporation
20071231	20080111	Phase Change	false	Preregistration for Migraine in USA (SC)
20080319	20080325	Licensing Status	true	Sumatriptan DosePro licensed to Desitin Pharmaceuticals in the EU
20080628	20080706	Scientific Update	true	Pharmacokinetics data from a Phase-I trial in healthy volunteers released by Zogenix (9090609)
20081031	20090220	Regulatory Status	false	Zogenix receives complete response letter from the FDA for sumatriptan needle-free injection in Migraine (9097956)

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PHS

Development Phases

Phase	Country	Indication	Route of Administration	Formulation	On Fast Track	Qualifiers and Comments
Marketed	Denmark	Migraine	SC	Injection	false	
Marketed	France	Migraine	SC	Injection	false	
Marketed	Germany	Migraine	SC	Injection	false	
Marketed	Norway	Migraine	SC	Injection	false	
Marketed	Sweden	Migraine	SC	Injection	false	
Marketed	United Kingdom	Migraine	SC	Injection	false	
Marketed	USA	Migraine	SC	Injection	false	
Registered	European Union	Migraine	SC	Injection	false	

Indexing (details) Cite

SU	**Subject**	Indoles; Small-molecules; Sulfonamides
SUBST	**Substance**	3-[2-(dimethyl-amino)ethyl]-N-methylindole-5-methanesulfonamide
SYN	**Drug synonym**	Needle-free subcutaneous sumatriptan, Sumatriptan DoseProTM, Sumatriptan Intraject®
MF	**Molecular formula**	C14H21N3O2S
GN	**Generic name**	Sumatriptan needle-free injection
TN	**Trade name**	Sumavel® DosePro(TM) (Migraine, European Union, Desitin Pharmaceuticals GmbH) Sumavel® DosePro(TM) (Migraine, USA, Zogenix)
TC	**Therapeutic class**	N2C1: Antimigraine triptans N02C-C01: Sumatriptan
DST	**Drug status**	Active
CO	**Company information**	Name: Aradigm Corporation, Public, Not-Large-Pharma Type: Pharmaceutical Role: Technology Provider Region: USA Name: Astellas Pharma US, Unknown, Not-Large-Pharma Type: Unknown Role: Market Licensee Region: USA Name: Desitin Pharmaceuticals GmbH, Private, Not-Large-Pharma Type: Pharmaceutical Role: Licensee Region: European Union Name: Mallinckrodt LLC, Public, Not-Large-Pharma Type: Pharmaceutical Role: Market Licensee Region: USA Name: Zogenix, Private, Not-Large-Pharma Type: Pharmaceutical Role: Originator Region: USA
TI	**Title**	Sumatriptan needle-free injection
HP	**Highest phase**	Marketed
LIC	**Licensing information**	Phase: unspecified, Available from: 2012-03-31, http://www.zogenix.com
LA	**Language**	English
DTYPE	**Document type**	Report
PUB	**Publication title**	Adis R&D Insight
PSTYPE	**Publication type**	Reports
PD	**Publication date**	Mar 19, 2013
DCRE	**Date created**	2005-09-28
DREV	**Date revised**	2013-03-19

	Source attribution	Adis R&D Insight, © Publisher specific
AN	**Accession number**	23278
	Document URL	http://search.proquest.com/professional/docview/1030584396?accountid=137296
FAV	**First available**	2012-08-02
UD	**Updates**	2012-08-13 2012-08-16 2013-03-21
	Database	Adis R&D Insight (1995 - current)

SEARCH FIELDS

You can use field codes on the Basic Search, Advanced Search, and Command Line Search pages to limit searches to specific fields. The table below lists the field codes for this file.

Field name	Field code	Example	Description and Notes
Accession number	AN	an(23278)	A unique document identification number assigned by the information provider.
All fields	ALL	all(potassium AND adverse events)	Searches all fields *except* the fulltext
All fields + text	--	potassium AND adverse events	Searches all fields including the fulltext
CAS® Registry number[1]	RN	rn(123447-62-1)	Also searchable using the Substance search field (SUBST).
Therapeutic classification[1]	TC	tc(antineoplastics)	Includes both the EPhMRA and WHO ATC therapeutic class codes.
Company	CO	co(3m healthcare)	Company names with their type, role (e.g. orginator, licensee) and region are presented. Search Originator as DOR(Zogenix) and Licensee as LCO(Desitin) or any company role as CO(Pfizer).
Country of launch/development	CLD	cld(brazil)	Displayed in the "DEVELOPMENT PHASE" section of the text.
Date created	DCRE	dcre(20111025) dcre(<20041223)	The date on which the information provider created the document.
Date revised	DREV	drev(20101118) drev(>=20101118)	The date on which the information provider revised the document.
Document text	TX	tx(intracellular calcium)	
Document title	TI	ti(riluzole)	This is usually the name of the drug.
Document type	DTYPE	dtype(report)	All documents contain "Report".
Drug status	DST	dst(active)	
Drug synonym	SYN	syn(ethinylestradiol)	
First available	FAV	fav(2012-12-05)	Indicates the first time the record was loaded onto PQD. It will not change regardless of how many times the record is subsequently reloaded, as long as the accession number does not change.
From database[2]	FDB	pub(nutrition) AND fdb(adisranddinsight) pub(nutrition) AND fdb(10000126)	Useful in multi-file searches to isolate records from a single file. FDB cannot be searched on its own; specify at least one search term then AND it with FDB.
Generic name	GN	gn(ezetimibe)	Also searchable using the Substance search field (SUBST).
Highest phase[1]	HP	hp(preclinical)	The highest phase the drug has reached anywhere in the world
History	HI	hi("regulatory status") hi(20120731) hi(2012-07-31)	Includes date, update, update date and brief details of milestones in the drug's development.
Indication	IND	ind(astrocytoma)	
Licensee	LCO	lco(shionogi pharma)	Also searchable using the Company search field (CO).
Licensing information	LIC	lic(europe)	
Mechanism of action[1]	MEC	mec(11-beta hydroxysteroid dehydrogenase	

[1] A Lookup/Browse feature is available for this field in the Advanced Search dropdown or in Browse Fields.

[2] Click the "Field codes" hyperlink at the top right of the Advanced Search page. Click "Search syntax and field codes", then click on "FDB command" to get a list of database names and codes that can be searched with FDB.

Field name	Field code	Example	Description and Notes
		inhibitors)	
Milestones	MRE	mre(orphan drug status)	Displayed in the History of Drug Development table in the text.
Molecular formula	MF	mf(c24h21f2no3)	
Origin of substance	OS	os(yes) os(no)	Fixed combination: yes or no
Originator	DOR	dor("sanofi-aventis")	Also searchable using the Company search field (CO).
Orphan substance	ORD	ord(bronchiectasis LNK usa)	
Pharmacokinetics	PK	pk("t (1/2) beta (h)")	
Phase[1]	PHS	phs(discontinued) phs(registered LNK "european union" LNK stroke)	Includes the phase, country, indication, route of administration, formulation, notes and indication of fast-track status. Use LNK or -- to link terms in the same row, e.g. PHS(marketed LNK european union LNK stroke)
Publication date	PD	pd(20110415) pd(>=20110415) pd(2010101 - 20110201)	Date range searching is supported.
Publication title	PUB	pub("adis r&d insight")	All Publication titles contain "Adis R&D Insight".
Publication type	PSTYPE	pstype(report)	All documents contain "Report".
Publication year	YR	yr(2007) yr(2009-2011) yr(>2009)	
References	REF	ref(Intraject needle-free system)	Includes cited authors' source information, language, country.
Route of administration	RO	ro(iv)	
Subject	SU	su(amides) su(migraine)	Broader terms describing the class of drug. Search includes indication, route of administration and mechanism of action.
Substance	SUBST	subst(5-chloro-6-[1-(2-iminopyrrolidinyl)methyl] uracil hydrochloride)	The chemical name of the drug.
Trade name	TN	tn(relistor)	Also searchable using the Substance search field (SUBST).
Updated	UD	ud(2012) ud(2012-08-13)	Date that documents were added or revised in ProQuest Dialog, to incorporate changes by an information provider.
Word count	WC	wc(>2500) wc(<2500)	

LIMIT OPTIONS

Limit options are quick and easy ways of searching certain common concepts. Check boxes are available for:

Full text, Drugs with a tradename, Documents with images

Short lists of choices are available for:

Phase, Highest phase, Drug status

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Therapeutic classification, Indication, Mechanism of action, Company

and in the fields drop-down only for:

Subject, Substance, Trade name

"Narrow Results By" Limiters

When results of a search are presented, the results display is accompanied by a list of "Narrow results by" options shown on the right-hand panel. Click on any of these options and you will see a ranked list showing the most frequently occurring terms in your results. Click on term(s) to include or exclude and apply them to ("narrow") your search results. "Narrow results by" limiters in Adis R&D Insight include

Full text, Therapeutic classification, Highest phase, Company, Mechanism of action, Indication, Publication date

Look Up Citation

If you need to trace a particular bibliographic reference, use the Look Up Citation feature. Find a link to this toward the top left of the Advanced Search page, or in the drop list under Advanced on any search form; click this link and you will go to a form where you can enter any known details of the citation, including document title, author, journal name, volume, issue, page, publication date, ISSN.

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