CBG MEB

PUBLIC ASSESSMENT REPORT of the Medicines Evaluation Board in the Netherlands

Zolmitriptan Sandoz tablet 2.5 mg and 5 mg, film-coated tablets Zolmitriptan Sandoz smelttablet 2.5 mg and 5 mg, orodispersible tablets Sandoz B.V., the Netherlands

zolmitriptan

This assessment report is published by the MEB pursuant Article 21 (3) and (4) of Directive 2001/83/EC. The report comments on the registration dossier that was submitted to the MEB and its fellow –organisations in all concerned EU member states.
It reflects the scientific conclusion reached by the MEB and all concerned member states at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation.
This report is intended for all those involved with the safe and proper use of the medicinal product, i.e. healthcare professionals, patients and their family and carers. Some knowledge of medicines and diseases is expected of the latter category as the language in this report may be difficult for laymen to understand.

This assessment report shall be updated by a following addendum whenever new information becomes available.

General information on the Public Assessment Reports can be found on the website of the MEB.

To the best of the MEB's knowledge, this report does not contain any information that should not have been made available to the public. The MAH has checked this report for the absence of any confidential information.

EU-procedure number: NL/H/1908/001-004/DC
Registration number in the Netherlands: RVG 106557-106560

31 August 2011

Pharmacotherapeutic group:	selective serotonin (5HT1) agonists
ATC code:	N02CC03
Route of administration:	oral
Therapeutic indication:	acute treatment of migraine headache with or without aura
Prescription status:	prescription only
Date of authorisation in NL:	31 May 2011
Concerned Member States:	Decentralised procedure with DE; 2.5 mg film-coated and orodispersible tablets only - AT
Application type/legal basis:	Directive 2001/83/EC, Article 10(1)

For product information for healthcare professionals and users, including information on pack sizes and presentations, see Summary of Product Characteristics (SPC), package leaflet and labelling.

I INTRODUCTION

Based on the review of the quality, safety and efficacy data, the member states have granted a marketing authorisation for Zolmitriptan Sandoz tablet 2.5 mg and 5 mg, film-coated tablets and Zolmitriptan Sandoz smelttablet 2.5 mg and 5 mg, orodispersible tablets from Sandoz B.V. The date of authorisation was on 31 May 2011 in the Netherlands. The product is indicated for acute treatment of migraine headache with or without aura.

A comprehensive description of the indications and posology is given in the SPC.

Zolmitriptan has been demonstrated to be a selective agonist for 5-HT1B/1D receptors mediating vascular contraction. Zolmitriptan has high affinity for human recombinant 5-HT1B and 5-HT1D receptors, and modest affinity for 5-HT1A receptors. Zolmitriptan has no significant affinity or pharmacological activity at other 5-HT receptor subtypes (5-HT2, 5-HT3, 5-HT4) or adrenergic, histaminic, muscarinic or dopaminergic receptors.

This decentralised procedure concerns a generic application claiming essential similarity with the innovator products Zomig 2.5 mg and 5 mg, tablets and Zomig Rapimelt 2.5 and 5 mg orodispersible tablets, which have been registered in Germany by AstraZeneca since 21 March 1997 and 7 March/17 December 2002 (original product). In the Netherlands, the innovator products Zomig and Zomig-ZIP 2,5 and 5 mg tablets (NL License RVG 31817-31820) have been registered since 10 April 2007 through MRP SE/H/0128/MR. In addition, reference is made to Zomig authorisations in the individual member states (reference product).

The marketing authorisation is granted based on article 10(1) of Directive 2001/83/EC.

This type of application refers to information that is contained in the pharmacological-toxicological and clinical part of the dossier of the authorisation of the reference product. A reference product is a medicinal product authorised and marketed on the basis of a full dossier, i.e. including chemical, biological, pharmaceutical, pharmacological-toxicological and clinical data. This information is not fully available in the public domain. Authorisations for generic products are therefore linked to the 'original' authorised medicinal product, which is legally allowed once the data protection time of the dossier of the reference product has expired. For this kind of application, it has to be demonstrated that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of the reference product. To this end the MAH has submitted bioequivalence studies in which the pharmacokinetic profile of the 5 mg products is compared with the pharmacokinetic profile of the reference products AscoTop 5 mg film-coated tablets and 5 mg orodispersible tablets, registered in Germany. A bioequivalence study is the widely accepted means of demonstrating that difference of use of different excipients and different methods of manufacture have no influence on efficacy and safety. These generic products can be used instead of their reference product.

No new pre-clinical and clinical studies were conducted, which is acceptable for this abridged application.

No scientific advice has been given to the MAH with respect to these products and no paediatric development programme has been submitted, as this is not required for generic medicinal products.

II SCIENTIFIC OVERVIEW AND DISCUSSION

II.1 Quality aspects

Compliance with Good Manufacturing Practice
The MEB has been assured that acceptable standards of GMP (see Directive 2003/94/EC) are in place for these product types at all sites responsible for the manufacturing of the active substance as well as for the manufacturing and assembly of this product prior to granting its national authorisation.

Active substance
The active substance is zolmitriptan, an established active substance however not described in any pharmacopoeia. It is a white to off-white crystalline powder, which is soluble in methanol, sparingly soluble in dichlormethane and practically insoluble in toluene. The active substance corresponds to the S-isomer of Zolmitriptan. The active substance exhibits polymorphism. One polymorphic form is used.

The Active Substance Master File (ASMF) procedure is used for the active substance. The main objective of the ASMF procedure, commonly known as the European Drug Master File (EDMF) procedure, is to allow valuable confidential intellectual property or 'know-how' of the manufacturer of the active substance (ASM) to be protected, while at the same time allowing the applicant or marketing authorisation holder (MAH) to take full responsibility for the medicinal product, the quality and quality control of the active substance. Competent Authorities/EMA thus have access to the complete information that is necessary to evaluate the suitability of the use of the active substance in the medicinal product.

Manufacturing process
The drug substance is produced by three manufacturers, either in a three-, four- or six-step process.
The active substance was adequately characterized by all ASMF holders and acceptable specifications have been adopted for the starting material, solvents and reagents.

Quality control of drug substance
The drug substance specification was established in house by the MAH. It is in line with the drug substance specifications of the ASMF holders with an additional requirement for particle size. The specification of the MAH is acceptable in view of the routes of synthesis and the various European guidelines.
Batch analytical data demonstrating compliance with the drug substance specification were provided for two batches obtained from each manufacturer.

Stability of drug substance
Stability data provided by the first manufacturer cover six full-scale batches stored at 25°C/60% RH (18 months) and 40°C/75% RH (six months). No specific trends or significant changes were observed. Stability data of the second ASMF holder include three full-scale batches stored at 25°C/60% RH (36 months) and 40°C/75% RH (six months). No significant changes were observed. Stability data provided for the third supplier cover five full-scale batches stored at 25°C/60% RH (3-18 months) and 40°C/75% RH (4-6 months). No specific trends or significant changes were observed.
The MAH applies an in-house re-test period of twelve months, which is acceptable based on the data provided.

Medicinal Product

Film-coated tablets
Composition
Zolmitriptan Sandoz tablet 2.5 mg is a yellow, round, biconvex, film-coated tablet with 'ZMT 2.5' debossed on one side.
Zolmitriptan Sandoz tablet 5 mg is a pink, round, biconvex, film-coated tablet with 'ZMT 5' debossed on one side.

The film-coated tablets are packed in Al/Al blisters.

The excipients are:
Tablet core - anhydrous lactose, colloidal anhydrous silica, microcrystalline cellulose, crospovidone, magnesium stearate
Tablet coating - hypromellose, hydroxypropylcellulose, macrogol, iron oxide yellow E172, titanium dioxide E171, talc; iron oxide red E172 (5 mg only).
Both formulations are dose proportional.

Pharmaceutical development
The development of the product has been described, the choice of excipients is justified and their functions explained. On laboratory scale, batches were prepared and the formulation was optimised. The choices for packaging and manufacturing process are justified. Composition, size, and manufacturing process of the generic batch used in the bioequivalence study correspond to those proposed for commercial production. Dissolution of the generic and reference product Zomig used in the bioequivalence study (both of the 5 mg strength) is similar in different media. Dissolution of the 2.5 mg and 5 mg strength of the generic product is similar in the three used buffers as well. The reference product was shown to be representative by comparing its dissolution profile to several batches of the 2.5 and 5 mg strength taken from various European markets. The impurity profiles of the generic and reference product are comparable.
Pharmaceutical development of the product was adequately performed. From a chemical pharmaceutical point of view, the generic and the reference product are considered to be similar.

Manufacturing process
The manufacturing process involves dry blending and sieving, slugging, milling, final blending, compression, film-coating and packaging. The manufacturing process has been adequately validated according to relevant European guidelines. Process validation data on the product was presented for three full scale batches of each strength.

Control of excipients
All excipients are of pharmacopoeial quality. These specifications are acceptable.

Quality control of drug product
The product specification includes tests for colour and appearance, water, identification of zolmitriptan, identification of colourants, assay, uniformity of dosage units, dissolution, related substances/degradation products, and microbiological quality. The release and shelf-life limits differ with regard to the limits for the assay and related substances/degradation products. This has been adequately justified. The drug product specification is acceptable. The analytical methods were adequately described and validated.
Batch analytical data from the proposed production site were provided on three full-scale batches of the 2.5 mg strength and on four full-scale batches of the 5 mg strength, demonstrating compliance with the release specification.

Stability of drug product
Stability data on the product has been provided for three full-scale batches of each strength stored at 25°C/60% RH (12-18 months) and 40°C/75% RH (six months). The conditions used in the stability studies are according to the ICH stability guideline. The batches were stored in Al/Al blisters and in bulk (the latter for 12 months at long term and three months at accelerated conditions).
At both storage conditions no significant changes were noted. Based on the provided stability data, the claimed shelf lives of two years for the blisters and 12 months for the bulk are acceptable. The claimed storage condition for the blisters of “Store in the original package in order to protect from moisture” is acceptable. The bulk storage below 25°C is approvable as well. Photostability of the unpacked tablets was demonstrated under ICH conditions. Additional stability data will be submitted to fully support the approved shelf life.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies

Lactose is the only excipient of animal origin. A BSE/TSE statement was provided confirming that the milk used for the manufacturing of pharmaceutical grade lactose is sourced from healthy animals under the same conditions as milk collected for human consumption.

Orodispersible tablets

Composition

Zolmitriptan Sandoz smelttablet 2.5 mg is a white, round tablet with 'ZMT 2.5' debossed on one side.
Zolmitriptan Sandoz smelttablet 5 mg is a white, round tablet with 'ZMT 5' debossed on one side.

The orodispersible tablets are packed in Al/Al blisters.

The excipients are: silicified microcrystalline cellulose, crospovidone, sodium hydrogen carbonate, anhydrous citric acid, colloidal anhydrous silica, mannitol (E421), sweet orange flavour, aspartame (E951), magnesium stearate.
Both formulations are dose proportional.

Pharmaceutical development

The development of the product has been described, the choice of excipients is justified and their functions explained. The formulation is based on the qualitative composition of the reference product. A direct compression approach was chosen. The formulation was optimized on the basis of short disintegration and appropriate stability. The choices for packaging and manufacturing process are justified. Composition, size, and manufacturing process of the generic batch used in the bioequivalence study correspond to those proposed for commercial production. Dissolution of the generic and reference product, Zomig Rapimelt, used in the bioequivalence study (both of the 5 mg strength) is similar in different media. Dissolution of the 2.5 mg and 5 mg strength of the generic product is similar in the three buffers as well. The reference product was shown to be representative by comparing its dissolution profile to several batches of the 2.5 and 5 mg strength taken from various European markets. The impurity profiles of the generic and reference product are comparable.
Pharmaceutical development of the product was adequately performed. From a chemical pharmaceutical point of view, the generic and the reference product are considered to be similar.

Manufacturing process

The manufacturing process involves dry blending and sieving of the active ingredient and powderous excipients, final blending, compression, batch homogenization and packaging.
The manufacturing process has been adequately validated according to relevant European guidelines. Process validation data on the product was presented for three full-scale batches of the 2.5 mg strength and four full-scale batches of the 5 mg strength.

Control of excipients

With the exception of the sweet orange flavour, all excipients are of pharmacopoeial grade. The specifications of the excipients are acceptable.

Quality control of drug product

The product specification includes tests for colour and appearance, disintegration, loss on drying, identification of Zolmitriptan, assay, uniformity of dosage units, dissolution, related substances/ degradation products and microbiological quality. The release and shelf life limits differ with regard to the limits for the assay and related substances/degradation products. The drug product specification is acceptable.
The analytical methods were adequately described and validated. Batch analytical data from the proposed production site were provided on three full-scale batches of the 2.5 mg strength and on four full-scale batches of the 5 mg strength, demonstrating compliance with the release specification.

Container Closure System

The Al/Al blisters were chosen to assure maximum protection from moisture. Stability test during development demonstrated that the blister material is adequate. It is comparable to the packaging

material of the reference product. The packaging materials are identical to the packaging materials used for the film-coated tablets except that the lidding foil is replaced by a peel-off foil of the same material.

Stability of drug product
Stability data on the product has been provided for three full-scale batches of the 2.5 mg strength stored at 25°C/60% RH (24 months) and 40°C/75% RH (6 months), and four full-scale batches of the 5 mg strength stored at 25°C/60% RH (24 months (2 batches), 18 months (1 batch), and 12 months (1 batch)) and 40°C/75% RH (6 months). The conditions used in the stability studies are according to the ICH stability guideline. The batches were stored in Al/Al blisters and in bulk (the latter for 12 months at long term and three months at accelerated conditions).
At both storage conditions but no significant changes were noted.
Based on the provided stability data, the claimed shelf lives of two years for the blisters and 12 months for the bulk are acceptable. The claimed storage condition for the blisters of "Store in the original package in order to protect from moisture" is acceptable. The bulk storage below 25°C is approvable as well. Photostability of the unpacked tablets was demonstrated under ICH conditions.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.

II.2 Non-clinical aspects

These products are generic formulations of Zomig and Zomig Rapimelt tablets, which are available on the European market. No new preclinical data have been submitted, and therefore the application has not undergone preclinical assessment. This is acceptable for this type of application.

Environmental risk assessment
These products are intended as a substitute for other identical products on the market. The approval of this product will not result in an increase in the total quantity of zolmitriptan released into the environment. It does not contain any component, which results in an additional hazard to the environment during storage, distribution, use and disposal.

II.3 Clinical aspects

Zolmitriptan is a well-known active substance with established efficacy and tolerability.

For this generic application, the MAH has submitted two bioequivalence studies in which the pharmacokinetic profile of the test products Zolmitriptan Sandoz tablet 5 mg and Zolmitriptan Sandoz smelttablet 5 mg (Sandoz B.V., the Netherlands) is compared with the pharmacokinetic profile of the reference product AscoTop® 5 mg, film-coated tablets and AscoTop 5 mg Schmelztabletten, orodispersible tablets (AstraZeneca GmbH, Germany).

The choice of the reference product
The choice of the reference products in the bioequivalence study has been justified by comparison of dissolution results and compositions of reference products in different member states.
The formula and preparation of the bioequivalence batch is identical to the formula proposed for marketing.

Bioequivalence study I - 5 mg film-coated tablets
Design
A single-dose, randomised, two-period, two-treatment, two-sequence, crossover bioequivalence study was carried out under fasted conditions in 36 healthy male subjects, aged 19-40 years. Each subject received a single dose (5 mg) of one of the 2 zolmitriptan formulations. The tablet was orally administered after an overnight fast. Meals were provided no less than 4 hours after drug administration. Water was

allowed *ad libitum* until 2 hours pre-dose and beginning 2 hours after drug administration. There were 2 dosing periods, separated by a washout period of 7 days.

Blood samples were collected pre-dose and at 0.17, 0.33, 0.5, 0.67, 0.83, 1.0, 1.17, 1.33, 1.67, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 8, 10, 12, 15 and 24 hours after administration of the products.

Analytical/statistical methods
The analytical method has been adequately validated and is considered acceptable for analysis of the plasma samples. The methods used in this study for the pharmacokinetic calculations and statistical evaluation are considered acceptable.

Results
One subject withdrew his consent after dosing of period 1 for personal reasons. The pharmacokinetic and statistical analysis was performed on data from 35 subjects.

Table 1. Pharmacokinetic parameters (non-transformed values; mean) of zolmitriptan under fasted conditions.

Treatment N=35	**AUC_{0-t}** ng.h/ml	**$AUC_{0-\infty}$** ng.h/ml	**C_{max}** ng/ml	**t_{max}** h	**$t_{1/2}$** h
Test	49.59	51.78	8.31	1.53	5.88
Reference	48.35	50.52	7.91	1.84	6.08
***Ratio (90% CI)**	1.02 (0.97-1.09)	1.02 (0.97-1.08)	1.05 (0.97-1.14)	--	--
CV (%)	14.2	12.9	20.4	--	--

$AUC_{0-\infty}$ area under the plasma concentration-time curve from time zero to infinity
AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours
C_{max} maximum plasma concentration
t_{max} time for maximum concentration
$t_{1/2}$ half-life

**ln-transformed values*

The 90% confidence intervals calculated for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max} are in agreement with those calculated by the MAH and are within the bioequivalence acceptance range of 0.80-1.25. Based on the pharmacokinetic parameters of zolmitriptan under fasted conditions, it can be concluded that Zolmitriptan Sandoz tablet 5 mg and AscoTop® 5 mg, film-coated tablets are bioequivalent with respect to rate and extent of absorption, and fulfil the bioequivalence requirements outlined in the relevant CHMP Note for Guidance.

Safety
Twenty-six of the thirty-six subjects experienced a total of 55 adverse events during the study. Twenty-eight adverse events were reported after the administration of the Test product and twenty-eight adverse events were reported after the administration of the Reference product. Two adverse events judged to be possibly related to the investigational products (blood potassium increased and ocular hyperemia) were unexpected. No SAEs were recorded in this study. No subject was withdrawn from the study because of an adverse event.

Bioequivalence study II - 5 mg orodispersible tablets
Design
A single-dose, randomised, two-period, two-treatment, two-sequence, crossover bioequivalence study was carried out under fasted conditions in 36 healthy male subjects, aged 19-40 years. Each subject

received a single dose (5 mg) of one of the 2 zolmitriptan formulations. The tablet was orally administered after an overnight fast. Meals were provided no less than 4 hours after drug administration. Water was allowed *ad libitum* until 2 hours pre-dose and beginning 2 hours after drug administration. Zolmitriptan orodispersible tablets were taken without water.
There were 2 dosing periods, separated by a washout period of 7 days.

Blood samples were collected pre-dose and at prior to and 0.25, 0.5, 0.75, 1, 1.33, 1.67, 2, 2.33, 2.67, 3, 3.33, 3.67, 4, 4.5, 5, 5.5, 6, 8, 10, 12, 15 and 24 hours after administration of the products.

Analytical/statistical methods
The analytical method has been adequately validated and is considered acceptable for analysis of the plasma samples. The methods used in this study for the pharmacokinetic calculations and statistical evaluation are considered acceptable.

Results
One subject was withdrawn by the physician after dosing of period 1 due to adverse events (chest pain and feeling hot of moderate intensity). The pharmacokinetic and statistical analysis was performed on data from 35 subjects.

Table 1. Pharmacokinetic parameters (non-transformed values; mean) of zolmitriptan under fasted conditions.

Treatment N=35	**AUC_{0-t}** ng.h/ml	**$AUC_{0-\infty}$** ng.h/ml	**C_{max}** ng/ml	**t_{max}** h	**$t_{1/2}$** h
Test	48.3	50.46	7.60	2.54	6.15
Reference	48.70	50.68	7.46	2.74	5.93
***Ratio (90% CI)**	0.99 (0.94-1.04)	1.00 (0.95-1.04)	1.02 (0.94-1.10)	--	--
CV (%)	12.5	11.0	19.9	--	--

$AUC_{0-\infty}$ area under the plasma concentration-time curve from time zero to infinity
AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours
C_{max} maximum plasma concentration
t_{max} time for maximum concentration
$t_{1/2}$ half-life

**ln-transformed values*

The 90% confidence intervals calculated for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max} are in agreement with those calculated by the MAH and are within the bioequivalence acceptance range of 0.80-1.25. Based on the pharmacokinetic parameters of zolmitriptan under fasted conditions, it can be concluded that Zolmitriptan Sandoz smelttablet 5 mg and AscoTop 5 mg Schmelztabletten, orodispersible tablets are bioequivalent with respect to rate and extent of absorption, and fulfil the bioequivalence requirements outlined in the relevant CHMP Note for Guidance.

Safety
Seventeen of the thirty-six subjects experienced a total of 41 adverse events during the study. Twenty-five adverse events were reported after the administration of the test product and seventeen adverse events were reported after the single dose administration of the Reference product. One adverse event (transaminases increased) associated with post-study laboratory test results, was imputed to both formulations. One adverse event judged to be possibly related to the investigational products (nightmare) was unexpected. No SAEs were recorded in this study.
The maximal intensity reported for these events ranged from mild to severe.

One subject was withdrawn from the study for safety reasons (chest pain and feeling hot of moderate intensity).

Food effect
Zolmitriptan may be taken without reference to food intake. From the literature it is known that food does not interact with the absorption of zolmitriptan. Therefore, a food interaction study is not deemed necessary. The bioequivalence study under fasting conditions is in accordance with CPMP/EWP/QWP/ 1401/98 Note for Guidance on the investigation of bioavailability and bioequivalence.

Biowaver
A biowaiver was granted for the 2.5 mg film-coated tablets and the 2.5 mg orodispersible tablets based on the bioequivalence study with the 5 mg film-coated and 5 mg orodispersible tablets. The following principles have been fulfilled:

- The pharmaceutical products are manufactured by the same manufacturer and process.
- The drug distribution has been shown to be linear over the therapeutic dose range.
- The qualitative composition of the different strengths is the same.
- The ratio between amounts of the active substance and excipients is the same.
- The dissolution profiles are similar under identical conditions and fast with >85% of a drug product dissolved within 15 min for the additional strength and the strengths of the batch used in the bioequivalence study.

The MEB has been assured that the bioequivalence studies have been conducted in accordance with acceptable standards of Good Clinical Practice (GCP, see Directive 2005/28/EC) and Good Laboratory Practice (GLP, see Directives 2004/9/EC and 2004/10/EC).

Risk management plan
Zolmitriptan first approved in 1997, and there is now more than 10 years post-authorisation experience with the active substance. The safety profile of zolmitriptan can be considered to be well established and no product specific pharmacovigilance issues were identified pre- or post authorisation which are not adequately covered by the current SPC. Additional risk minimisation activities have not been identified for the reference medicinal product. The MAH has a pharmacovigilance system at their disposal, which is based on the current European legislation. Routine pharmacovigilance activities are sufficient to identify actual or potential risks and a detailed European Risk Management Plan is not necessary for this product.

Product information

SPC
The content of the SPC approved during the decentralised procedure is in accordance with that accepted for the reference products Zomig and Zomig-ZIP (SE/H/0128/01-04/H/033).

Readability test
The package leaflet has not been evaluated via a user consultation study. A bridging report was submitted in which reference is made to a comparable product, rizatriptan. The justification for absence of a user test regarding text and layout of the PIL was considered sufficient and was accepted by the member states.

III OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

Zolmitriptan Sandoz tablet 2.5 mg and 5 mg, film-coated tablets and Zolmitriptan Sandoz smelttablet 2.5 mg and 5 mg, orodispersible tablets have a proven chemical-pharmaceutical quality and are generic forms of Zomig and Zomig Rapimelt. Zomig is a well-known medicinal product with an established favourable efficacy and safety profile.

Bioequivalence has been shown to be in compliance with the requirements of European guidance documents.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The SPC is consistent with that of the reference product. The SPC, package leaflet and labelling are in the agreed templates.

The Board followed the advice of the assessors.

There was no discussion in the CMD(h). Agreement between member states was reached during a written procedure. The member states, on the basis of the data submitted, considered that essential similarity has been demonstrated for Zolmitriptan Sandoz tablet 2.5 mg and 5 mg, film-coated tablets and Zolmitriptan Sandoz smelttablet 2.5 mg and 5 mg, orodispersible tablets with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finished on 10 May 2011. Zolmitriptan Sandoz tablet 2.5 mg and 5 mg and Zolmitriptan Sandoz smelttablet 2.5 mg and 5 mg were authorised in the Netherlands on 31 May 2011.

A European harmonised birth date has been allocated (7 March 1997) and subsequently the first data lock point for zolmitriptan is March 2012. The first PSUR will cover the period from May 2011 to March 2012, after which the PSUR submission cycle is 3 years.

The date for the first renewal will be: 23 December 2015.

The following post-approval commitment has been made during the procedure:

Quality - medicinal product

- The MAH committed to provide additional stability data fully covering the claimed shelf life for the film-coated tablets.

List of abbreviations

ASMF	Active Substance Master File
ATC	Anatomical Therapeutic Chemical classification
AUC	Area Under the Curve
BP	British Pharmacopoeia
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence Interval
C_{max}	Maximum plasma concentration
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CV	Coefficient of Variation
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EU	European Union
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
MEB	Medicines Evaluation Board in the Netherlands
OTC	Over The Counter (to be supplied without prescription)
PAR	Public Assessment Report
Ph.Eur.	European Pharmacopoeia
PIL	Package Leaflet
PSUR	Periodic Safety Update Report
SAE	Serious Adverse Event
SD	Standard Deviation
SPC	Summary of Product Characteristics
$t_{½}$	Half-life
t_{max}	Time for maximum concentration
TSE	Transmissible Spongiform Encephalopathy
USP	Pharmacopoeia in the United States

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Scope	Procedure number	Type of modification	Date of start of the procedure	Date of end of the procedure	Approval/ non approval	Assessment report attached