COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Egotux 12.5 mg, 25 mg, 37.5 mg and 50 mg hard capsules (sunitinib)

NL/H/5558/001-004/DC

Date: 26 May 2023

This module reflects the scientific discussion for the approval of Egotux 12.5 mg, 25 mg, 37.5 mg and 50 mg hard capsules. The procedure was finalised on 21 November 2022. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
CQAs	Critical Quality Attributes
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Egotux 12.5 mg, 25 mg, 37.5 mg and 50 mg hard capsules, from Genepharm S.A.

The product is indicated for:

Gastrointestinal stromal tumour (GIST)
Indicated for the treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumour (GIST) in adults after failure of imatinib treatment due to resistance or intolerance.

Metastatic renal cell carcinoma (MRCC)
Indicated for the treatment of advanced/metastatic renal cell carcinoma (MRCC) in adults.

Pancreatic neuroendocrine tumours (pNET)
Indicated for the treatment of unresectable or metastatic, well-differentiated pancreatic neuroendocrine tumours (pNET) with disease progression in adults.

A comprehensive description of the up-to-date indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC, which concerns a generic application.

The concerned member state (CMS) involved in this procedure was Greece.

In this decentralised procedure, essential similarity is proven between the new product and the innovator product Sutent hard capsules which has been registered in the EEA via a centralised procedure (EU/1/06/347). The first marketing authorisation was granted on 24 July 2006 (for Sutent 12.5 mg, 25 mg and 50 mg), later an additional strength was added via a marketing authorisation extension in May 2009 (Sutent 37.5 mg).

The drug substance used in Egotux, hard capsules is sunitinib base, whereas the drug substance used in Sutent is sunitinib malate. As per Directive 2001/83/EC and its amendments "The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance".

Similarity assessment
According to Article 8(1) of Regulation (EC) No 141/2000, no marketing authorisation can be granted for a product similar to an orphan medicinal product for a period of ten years, when this concerns a similar medicinal product with the same therapeutic indication. The reference product was originally designated as an orphan medicine for the orphan indications renal cell carcinoma and malignant gastrointestinal stromal tumours. Sutent, hard capsules was withdrawn from the Community register of orphan medicinal products in July 2008 upon request of the marketing authorisation holder (MAH).

The MAH has provided a similarity assessment between Egotux, hard capsules and the current orphan products authorised in the EU. These orphan products and their respective indications are:

- Indicated for the treatment of gastro-entero-pancreatic neuroendocrine tumours
    - Lutathera (lutetium (177Lu) oxodotreotide), EU1/17/1226.
    - Onivyde pegylated liposomal (irinotecan in a pegylated liposomal formulation), EU/1/16/1130.
- Indicated for the treatment of gastrointestinal stromal tumour (GIST):
    - Ayvakyt (avapritinib), EU/1/20/1473.
- Indicated for the diagnosis of gastro-entero-pancreatic neuroendocrine tumours:
    - Somakit TOC, EU/1/16/1141 (for diagnostic use only).

The assessment took into account the therapeutic indication, mechanism of action and principal molecular structural features. After consideration of the MAH arguments, Egotux is not considered similar to the orphan products with regard to the therapeutic indication (as defined in Article 3 of Commission Regulation (EC) No. 847/2000). Therefore, the existence of any market exclusivity for Lutathera, Onivyde pegylated liposomal, SomaKit TOC, in the treatment of gastro-entero-pancreatic neuroendocrine tumours and Ayvakyt in the treatment of gastrointestinal stromal tumour (GIST), does not prevent the granting of the marketing authorisation for Egotux, hard capsules.

II. QUALITY ASPECTS

II.1 Introduction

Egotux are hard capsules containing 12.5, 25, 37.5, or 50 mg sunitinib base as active substance. The capsules of the different strengths can be distinguished by colour, size and imprinting and are as follows:

- The 12.5 mg strength are hard capsules with an orange cap and orange body, printed with white ink ‘SB 12.5’ and a white line on the body, containing yellow to orange granules, with a nominal length of approximately 14.3 mm.
- The 25 mg strength are hard capsules with a caramel cap and orange body, printed with white ink ‘SB 25’ and a white line on the body, containing yellow to orange granules, with a nominal length of approximately 15.9 mm.
- The 37.5 mg strength are hard capsules with a yellow cap and yellow body, printed with black ink ‘SB 37.5’ and a black line on the body, containing yellow to orange granules, with a nominal length of approximately 18.0 mm.
- The 50 mg strength are hard capsules with a caramel cap and caramel body, printed with white ink ‘SB 50’ and a white line on the body, containing yellow to orange granules, with a nominal length of approximately 19.4 mm.

The excipients are:
Capsule content - cellulose microcrystalline E460, croscarmellose sodium E468, mannitol E421, povidone K-30 E1201 and magnesium stearate E470b.

Capsule shell - gelatin, titanium dioxide E171, red iron oxide E172 (for 12.5 mg, 25 mg and 50 mg capsules), yellow iron oxide E172 (for 25 mg, 37.5 mg, and 50 mg capsules), black iron oxide E172 (for 25 mg and 50 mg capsules), printing ink (white for 12.5 mg, 25 mg and 50 mg capsules and black for 37.5 mg capsules).

White printing ink - shellac E904, titanium dioxide E171 and propylene glycol.

Black printing ink - shellac E904, propylene glycol, concentrated ammonia solution, black iron oxide, and potassium hydroxide.

The capsule content of the different strengths are dose proportional.

The hard capsules are packaged in three types of packaging:

- White High Density Polyethylene (HDPE) bottles of 30 hard capsules closed with a white HDPE child resistant screw cap with a multilayer sealing pad.
- White HDPE bottles of 30 hard capsules closed with a white HDPE child resistant screw cap with a multilayer sealing pad; a silica gel desiccant canister is included in the primary container.
- Transparent PVC/PCTFE/aluminium blister of 28 hard capsules.

II.2 Drug Substance

The active substance is sunitinib base, an established active substance that is not described in any pharmacopoeia. The active substance is a yellow to orange crystalline powder which is not hygroscopic. The solubility in aqueous solution is pH dependent. Below pH 6, sunitinib base is soluble in aqueous solution, whereas above pH 7 it is only sparingly soluble in water. Sunitinib contains no chiral centres. More than 30 forms of sunitinib base are known in the literature. For Egotux, one polymorphic form is consistently produced by the manufacturer. The stability of this polymorphic form during storage of the drug substance has been demonstrated.

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 manufacturing process consists of several steps for synthesis and a final purification step. In the synthesis, no class 1 organic solvents are used. Adequate specifications have been adopted for starting/intermediates materials, solvents and reagents. The active substance has been adequately characterised and the manufacturing process is described in sufficient detail.

Quality control of drug substance
The active substance specification has been appropriately justified and are considered adequate to control the quality. Batch analytical data demonstrating compliance with this specification have been provided for three batches.

Stability of drug substance
The re-test period and storage conditions for the active substance as stated in the ASMF are also applied by the drug product manufacturer. The re-test applied by the ASMF holder, at the stated store conditions, has been substantiated with 36 months long-term and 6 months accelerated stability data from three commercial scale batches and is found acceptable.

II.3 Medicinal Product

Pharmaceutical development
The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

The drug product Egotux consist of hard gelatin capsules intended for immediate release and is available in four strengths (12.5 mg, 25 mg, 37.5 mg and 50 mg). The current product composition does not fully resemble the reference product Sutent. The salt form of the drug substance in Egotux is a base, while the malate form is used in Sutent. Furthermore, for Egotux microcrystalline cellulose is used, whereas this excipient is not present in Sutent. Formulation development studies have been performed to enhance dissolution, physical attributes and stability of the drug substance in the finished dosage form. An initial risk assessment was conducted on the potential impact of formulation variables on the Critical Quality Attributes (CQAs), then an updated risk assessment was performed in accordance with the ICH Q8 (R2) guidance. The related development trials have been sufficiently described. Overall, the development of the product has been described, the choice of excipients is justified and their functions explained.

In vitro dissolution tests complementary to the bioequivalence studies performed with the 50 mg strength, have been sufficiently addressed. A biowaiver for the additional strengths was granted, see details in section IV.2. The developed routine dissolution testing method is acceptable. The discriminatory power of the method has been sufficiently demonstrated. In general, an acceptable control strategy for commercial scale has been developed.

Manufacturing process
The manufacturing process is classified as standard and mainly consists of wet granulation, mixing and encapsulation. The manufacturing process has been validated according to

relevant European/ICH guidelines. Process validation data on the product have been submitted for three production scaled batches per strength. This is acceptable.

Control of excipients

The control of the excipients in the capsule content and capsule shell are in agreement with the Ph. Eur. requirements. The specifications for cellulose microcrystalline contain additional in-house test and specifications for Particle Size Distribution (PSD). In-house specifications for the hard gelatin capsules have been submitted. The specifications for excipients are considered acceptable.

Quality control of drug product

The finished product specifications are adequate to control the relevant parameters for the dosage form. The specification includes tests for appearance, identification, disintegration, dissolution, average fill weight, water content, assay, related substances (incl. total impurities), uniformity of dosage units (by content uniformity for 12.5 mg strength and by mass variation for 25, 37.5 and 50 mg strengths) and microbial quality. The release and shelf life specifications differ with regard the acceptance criteria for water content and impurities. The proposed specification is considered acceptable. Limits in the specification have been justified and are considered appropriate for adequate quality control of the product.

An adequate nitrosamines risk evaluation report has been provided. No risk for presence of nitrosamines in the drug product was identified.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data for three bulk capsules batches per strength from the proposed production site have been provided, demonstrating compliance with the specification. For the microbiological quality tests, the results for nine drug product batches per strength (3 batches per type of packaging) were submitted. All batches comply with the proposed specification.

Stability of drug product

Stability data on the product have been provided for three batches per strength and per proposed packaging material, stored at 25°C/ 60% RH (long term, 24 months) and 40°C/75% RH (accelerated, 6 months). The stability was tested in accordance with applicable European guidelines. All the tested parameters under long term and accelerated conditions remain within the proposed specification. Photostability study has been performed in accordance with the ICH. The directly exposed drug product and drug product in primary packaging are considered photo stable. On basis of the stability data submitted, a shelf life was granted for 36 months. Warning on protection from moisture is applicable, as the drug product concerns gelatin capsules, which are known to be sensitive to moisture. The labelled conditions are: "*This medicinal product does not require any special temperature storage conditions. Store in the immediate container to protect from moisture".*

In-use stability data for drug product (packed in HDPE bottles with a plastic child resistant screw cap, without desiccant) has been submitted. The lowest and highest strengths were

included in the study (12.5 and 50 mg, two batches per strength). Based on the reported results no in-use shelf life is considered necessary.

Container Closure System
The proposed packaging materials are well known and usual for this type of product. Sufficient information is provided on the container closure system. Furthermore, it has been tested and confirmed that the child-resistant screw cap on the HDPE container packaging complies with ISO 8317:2015.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
Scientific data and/or certificates of suitability issued by the EDQM for the excipient gelatin (used for the empty hard capsules) have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via medicinal products has been satisfactorily demonstrated.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Egotux has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.

No post-approval commitments were made.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

Since Egotux is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment was therefore not deemed necessary.

III.2 Discussion on the non-clinical aspects

This product is a generic formulation of Sutent which is available on the European market. Reference was made to the preclinical data obtained with the innovator product. A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which was based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. Therefore, the member states agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Introduction

Sunitinib is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The member states agreed that no further clinical studies are required, besides the two bioequivalence studies which are discussed below.

IV.2 Pharmacokinetics

The MAH conducted two bioequivalence studies in which the pharmacokinetic profile of the test product Egotux 50 mg from Genepharm S.A., Greece was compared with the pharmacokinetic profile of the reference product Sutent (sunitinib malate) 50 mg hard capsules from Pfizer Ltd, United Kingdom (study fasted conditions) and Pfizer Europe MA EEIG (study fed conditions). For the lower strengths 12.5 mg, 25 mg, 37.5 mg, a biowaiver was applicable. The choice of the reference product in the bioequivalence study has been justified by comparison of dissolution study results and composition. The formula and preparation of the bioequivalence batch is identical to the formula proposed for marketing.

Biowaiver

The following general requirements must be met where a waiver for additional strengths is claimed, according to the EMA Bioequivalence guideline CPMP/EWP/QWP/ 1401/98Rev.1/Corr**:

a. the pharmaceutical products are manufactured by the same manufacturing process,
b. the qualitative composition of the different strengths is the same,
c. the composition of the strengths are quantitatively proportional, i.e. the ratio between the amount of each excipient to the amount of active substance(s) is the same for all strengths (for immediate release products coating components, capsule shell, colour agents and flavours are not required to follow this rule),
d. appropriate *in vitro* dissolution data should confirm the adequacy of waiving additional *in vivo* bioequivalence testing.

The dissolution profiles of the bio batch test 50 mg and the three additional lower strengths (using 12 units for each respective strength per test) were studied at pH 1.2 HCl 0.1N, pH 4.5 acetate buffer and pH 6.8 phosphate buffer. For this study, the same batches of the test and reference product were used as in the BE study. Dissolution similarity at pH 1.2, 4.5 and 6.8 between the test 50 mg and the three additional lower strengths has been demonstrated, since all strengths dissolved more than 85% within 15 minutes at pH 1.2 and f_2 values were more than 50 at pH 4.5 and pH 6.8. With these results, the requirements for the biowaiver for the additional strengths have been met.

Bioequivalence Study, fasted conditions

Design

A randomised, open-label, balanced, two-treatment, two-period, two-sequence, single-dose, crossover bioequivalence study was carried out under fasted conditions in 31 healthy male

subjects, aged 22-43 years. Each subject received a single dose (50 mg) of one of the two sunitinib formulations. The tablet was orally administered with approximately 240 mL water after an overnight fasting period of at least ten hours, followed by a four hours post-dose fasting period. Drinking water was not allowed from one hour before dosing until one hour post-dose, except for the water given by the dose. There were two dosing periods, separated by a washout period of 28 days.

Blood samples were collected pre-dose and at 1, 3, 4, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9, 10, 10.5, 11, 11.5, 12, 13, 14, 16, 20, 24, 36, 48 and 72 hours after administration of the products.

The design of the study is acceptable. Food has no effect on the bioavailability of sunitinib. Dosing under fasting conditions is justified as the immediate release formulation can be taken with or without food.

Results
The 31 subjects that participated in the study completed both periods and were eligible for pharmacokinetic analysis.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} (median, range)) of sunitinib, 50 mg under fasted conditions.

Treatment N=31	**$AUC_{0\text{-}72\ hrs}$ (ng/mL.h)**	**C_{max} (ng/mL)**	**t_{max} (h)**
Test	1482 ± 338	41.6 ± 9	7.5 (5.5– 12.0)
Reference	1480 ± 304	41.8 ± 9	6.5 (5.0 – 14.0)
***Ratio (90% CI)**	1.00 (0.97 –1.03)	1.00 (0.95 – 1.04)	-

$AUC_{0\text{-}\infty}$	Area under the plasma concentration-time curve from time zero to infinity
$AUC_{0\text{-}t}$	Area under the plasma concentration-time curve from time zero to the last measurable plasma concentration (t=72 hours)
C_{max}	Maximum plasma concentration
t_{max}	Time after administration when maximum plasma concentration occurs
CI	Confidence interval

**ln-transformed values*

<u>Bioequivalence Study, fed conditions</u>
Design
A randomised, open-label, balanced, two-treatment, two-period, two-sequence, single-dose, crossover bioequivalence study was carried out under fed conditions in 32 healthy male subjects, aged 18-39 years. After an overnight fast period of at least 10 hours, subjects consumed a standardised, high-fat, high-calorie breakfast of 946 Kcal in 30 minutes and exactly 30 minutes before dosing. Each subject received a single dose (50 mg) of one of the two sunitinib formulations. The tablet was orally administered with approximately 240 mL water. There were two dosing periods, separated by a washout period of 28 days.

Blood samples were collected pre-dose and at 1, 3, 4, 5, 6, 7, 7.5, 8, 8.5, 9, 9.33, 9.67, 10, 10.33, 10.67, 11, 11.5, 12, 13, 14, 18, 24, 36, 48 and 72 hours after administration of the products.

The design of the study is acceptable. According to the Bioequivalence Guidance a single dose study under fasting conditions using the highest strength is considered appropriate because food has no effect on the bioavailability of sunitinib. However, this is referring to the drug substance sunitinib malate (Sutent) while Egotux contains sunitinib base. There are indications that sunitinib base is significantly less soluble than sunitinib malate at pH 6.8. Food intake increases the pH in the stomach and may have an effect on the absorption of the sunitinib base. Hence, the performance of a bioequivalence study under fed conditions is justified.

Results

32 subjects were dosed in period 1 and 30 subjects in period 2. Three subjects withdrew in period 1, two of them due to mild adverse events, one due to vomiting after administration of the reference product and one due to dizziness after administration of the test product. The third subject withdrew for personal reasons. A total of 29 subjects completed the study and were eligible for pharmacokinetic analysis.

Table 2. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} (median, range)) of sunitinib, 50 mg under fed conditions.

Treatment N=29	**$AUC_{0-72hrs}$ (ng/mL.h)**	**C_{max} (ng/mL)**	**t_{max} (h)**
Test	1754 ± 334	44.9 ± 10.0	9.2 (5.0 – 14.0)
Reference	1715± 281	43.3 ± 8.8	9.3 (5.0-12.0)
***Ratio (90% CI)**	1.02 (0.98 –1.06)	1.03 (1.00– 1.07)	-

$AUC_{0-\infty}$	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 the last measurable plasma concentration (t=72 hours)
C_{max}	Maximum plasma concentration
t_{max}	Time after administration when maximum plasma concentration occurs
CI	Confidence interval

**ln-transformed values*

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.

Conclusion on bioequivalence studies:

The 90% confidence intervals calculated for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max} are within the bioequivalence acceptance range of 0.80 – 1.25, for both studies, under fed and fasted conditions. Based on the submitted bioequivalence studies, Egotux 50 mg is considered bioequivalent with Sutent, 50 mg. Furthermore, the results of the bioequivalence studies with

the 50 mg formulation can be extrapolated to the other Egotux strengths, 12.5 mg, 25 mg, 37.5 mg, according to conditions in Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1/Corr, section 4.1.6.

The MEB has been assured that the bioequivalence study has 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).

IV.3 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Egotux.

Table 2. Summary table of safety concerns as approved in RMP

Important identified risks	• Cardiotoxicity
	  ○ Torsade de pointes
	  ○ Left ventricular dysfunction/Heart failure
	  ○ Pericardial events
	  ○ Cardiac ischemic events
	• Reversible Posterior Leukoencephalopathy Syndrome
	• Hepatic failure
	• Osteonecrosis of the jaw
	• Severe cutaneous adverse reactions
	• Renal failure

Important potential risks	• Carcinogenicity
Missing information	• Severe hepatic impairment

The member states agreed that routine pharmacovigilance activities and routine risk minimisation measures are sufficient for the risks and areas of missing information.

IV.4 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Sutent. The MAH demonstrated through two bioequivalence studies that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of this reference product. Risk management is adequately addressed. This generic medicinal product can be used instead of the reference product.

V. USER CONSULTATION

The package leaflet (PL) has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PL was English. The test consisted of: a pilot test with 3 participants, followed by two rounds with 10 participants each. The questions covered the following areas sufficiently: traceability, comprehensibility and applicability. The results show that the PL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Egotux 12.5 mg, 25 mg, 37.5 mg and 50 mg hard capsules, have a proven chemical-pharmaceutical quality and are generic forms of Sutent 12.5 mg, 25 mg, 37.5 mg and 50 mg. Sutent 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 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 Egotux with the reference product, and have therefore granted a marketing authorisation. The decentralised/mutual recognition procedure was finalised with a positive outcome on 21 November 2022.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
-	-	-	-	-	-