IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Xylocaine 20mg/g Gel
Lidocaine Hydrochloride Monohydrate
PA1691/037/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Xylocaine 20mg/g Gel, from Aspen Pharma Trading Limited on 26th June 2026 for the following indications:

Xylocaine 20mg/g Gel *is indicated as surface anaesthetic and lubricant for adults and adolescents aged 12 years and above:*

- *The male and female urethra during cystoscopy, catheterisation, exploration by sound and other endourethral procedures.*
- *Nasal and pharyngeal cavities in endoscopic procedures such as gastroscopy and bronchoscopy.*
- *During proctoscopy and rectoscopy*
- *Tracheal Intubation.*

This application for a marketing authorisation was submitted in accordance with Article 10a of Directive 2001/83/EC as amended, as a well-established use application. For this type of application, applicants need to demonstrate that the active substance of the medicinal product has been in well-established medicinal use within the Community for at least ten years in the specific therapeutic use. The results of non-clinical and clinical trials are replaced by detailed references to published scientific literature.

Ireland was Reference Member State RMS) in the decentralised procedure and the Concerned Member States (CMSs) were Malta and Poland.

Xylocaine 20mg/g Gel is subject to prescription which may not be renewed.

No scientific advice was given to the applicant.

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA's website at www.hpra.ie

Name of the product	Xylocaine 20mg/g Gel
Name(s) of the active substance(s) (INN)	Lidocaine Hydrochloride Monohydrate
Pharmacotherapeutic classification	(ATC code) N01BB02
Pharmaceutical form and strength(s)	20mg/g Gel
Marketing Authorisation Number(s) in Ireland (PA)	PA1691/037/001
Marketing Authorisation Holder	Aspen Pharma Trading Limited
MRP/DCP No.	IE/H/1332/001/DC
Reference Member State	IE
Concerned Member State	MT, PL

II. QUALITY ASPECTS

II.1. Introduction

This application is for Xylocaine 20mg/g Gel.

II.2 Drug substance

The active substance is Lidocaine Hydrochloride Monohydrate; an established active substance described in Pharmacopoeia (Ph. Eur. Monograph number 227) and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specification is considered adequate to control the quality and meets current pharmacopeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

Lidocaine Hydrochloride 20mg/g Gel (Lidocaine 2% Gel) is a clear to almost clear slightly coloured, highly viscous liquid, packed in collapsible aluminium tube, internally coated and closed with a tube cap. Lidocaine Hydrochloride 20mg/g Gel is a sterile gel intended for single use only.

The drug product contains 0.6g of lidocaine hydrochloride per 30g unit.

The excipients in the medicinal product are listed in section 6.1 of the SmPC.
A visual description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development

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

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process has been validated according to relevant European/ICH guidelines, and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients/*Ancillary Substances*)

All ingredients comply with Ph. Eur. or are adequately controlled by the manufacturer's specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopeial monograph for the dosage form and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site(s) have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the packaging complies with Ph. Eur./EU legislation for use with foodstuffs requirements.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of Xylocaine 20mg/g Gel.

III. NON-CLINICAL ASPECTS

III.1 Introduction

The active substance, lidocaine, a short-acting local anaesthetic of the amide type with a rapid onset of action, has been available on the European/Irish market for several decades. Non-clinical data have been superseded by clinical experience.

The nonclinical data have been collected from the published scientific literature, which is based on the results of experiments conducted by numerous independent investigators, there has been no well-structured testing strategy. Therefore, the GLP status of the reported studies is unknown.

III.2 Pharmacology

The primary pharmacodynamics of lidocaine are well-established. Like other local anaesthetics, topical anaesthetic agents such as lidocaine reversibly block nerve conduction near site of application by targeting free nerve endings in the dermis or mucosa, thereby producing temporary loss of sensation in a limited area. Nerve impulse conduction is blocked by decreasing nerve cell membrane permeability to sodium ions, possibly by competing with calcium-binding sites that control sodium permeability. This change in permeability decreases depolarization and increases excitability threshold until the ability to generate an action potential is lost.
Secondary pharmacology studies were not provided. Considering the extensive clinical experience with lidocaine the lack of secondary pharmacology studies is acceptable.

III.3 Pharmacokinetics

Lidocaine is absorbed rapidly after parenteral administration and from mucous membranes. Absorption is also rapid through damaged skin and from the intestine and respiratory tracts. Absorption through intact skin is poor. Lidocaine is rapidly absorbed from injection sites including muscle.
Lidocaine is almost completely metabolised before excretion in all species, with the liver as the primary site of metabolism. The major metabolites excreted in urine in man are conjugates of 4-hydroxy-2,6-DMA, accounting for about 70% of the dose.
There are differences in the pharmacokinetic properties of lidocaine between species. However, differences in local anaesthetic action between animals and humans are more likely to be affected by the physiology and anatomy of the nerves blocked than by differences in the rate of drug metabolism and excretion.

III.4 Toxicology

Lidocaine is an effective local anaesthetic with an intermediate duration of action. The most evident toxicity observed, convulsions, is due to the effect on the CNS. Cardiotoxicity was low at non-convulsant doses but increased at convulsive and superconvulsive doses, leading to arrhythmia or cardiac collapse in some of the animals. Lidocaine is not cardiotoxic and neurotoxic at clinically used concentrations. The neurotoxic and cardiotoxic effects of lidocaine could be reduced by tranquillisers such as diazepam.

Nonclinical studies did not show an effect of lidocaine on fertility or early embryonic development.

Genotoxicity studies showed that lidocaine does not pose a genotoxic risk to humans.

Carcinogenicity studies have not been performed with lidocaine, as according to guideline ICH S1A, they are not needed for pharmaceuticals administered infrequently or for short duration of exposure. However, one of the main metabolites of lidocaine, 2,6-DMA, has been recognised as a possible carcinogen in rats; therefore, it is included in Section 5.3 of the SmPC.

III.5 Ecotoxicity/environmental risk assessment

An environmental risk assessment was provided for lidocaine in accordance with the guideline (CHMP/SWP/4447/00 corr2). Lidocaine is not a PBT substance as log Kow does not exceed 4.5. The PECsw value was greater than the action limit of 0.01 µg /L. Phase-II Tier A evaluations concluded that that lidocaine and/or its metabolites are unlikely to represent a risk to the aquatic environment.

III.6 Discussion on the non-clinical aspects

As lidocaine is a well-known active substance, this is a bibliographic application with no new non-clinical studies conducted by the applicant. The submitted overview of the available non-clinical pharmacodynamic, pharmacokinetic and toxicological data is acceptable. As lidocaine is a widely used, well-known active substance, the applicant has not provided additional nonclinical studies, and further studies are not required. Lidocaine is not expected to pose a risk to the environment.

IV. CLINICAL ASPECTS

IV.1 Introduction

Lidocaine hydrochloride monohydrate is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided for this well-established use application, which is based on scientific literature. The overview justifies why there is no need to generate additional clinical data.

IV.2 Pharmacokinetics

Absorption
The rate and extent of lidocaine absorption after topical application to mucous membranes are dependent on the concentration and total dose administered, the site of administration and duration of administration. In general, the rate of absorption after topical administration is greatest after intratracheal or bronchial administration. Such applications can therefore lead to rapidly rising or excessively high plasma concentrations, with an increased risk of toxic symptoms such as convulsions. Lidocaine is also rapidly absorbed from the gastrointestinal tract, although little of the drug enters the circulation due to the first-pass effect in the liver. Blood concentrations of lidocaine hydrochloride after instillation of the gel in the intact urethra and bladder in doses up to approximately 800 mg in adults are fairly low and below the levels at which systemic effects or toxicity are likely to occur. Lesions of the urethral mucosa and/or surface enlargement due to urethral dilation can lead to increased absorption of lidocaine.

Bridging to products used in literature
No bioequivalence studies have been conducted between products used in literature or authorised similar formulations and the proposed medicinal product. However, detailed comparison tables were provided confirming that the proposed product is identical in both qualitative and quantitative terms to other similar products already in the market.

Distribution
Normally, about 65% of lidocaine is bound to plasma proteins. Amide-type local anaesthetics are mainly bound to alpha-1-acid glycoprotein (AAG) and also to albumin.

Lidocaine crosses the blood-brain barrier and placenta, probably due to passive diffusion.

Biotransformation
Lidocaine is mainly eliminated via hepatic metabolism. In humans, it is primarily metabolised via N dealkylation to monoethylglycinexylidide (MEGX), followed by hydrolysis to 2,6-xylidine and hydroxylation to 4-hydroxy-2,6-xylidine. MEGX can also be further metabolised via N-dealkylation to glycine xylidide (GX). The pharmacological/toxic action of MEGX and GX is comparable with, but less potent than, that of lidocaine. GX has a longer half-life (about 10 hours) than lidocaine and it can accumulate during prolonged administration.

Elimination
In healthy adults, the elimination half-life of lidocaine is 1.5 – 2 hours. The elimination half-life is about 10 hours for glycine xylidide and 2 hours for monoethylglycinexylidide.
About 90% of administered lidocaine is excreted in the form of various metabolites and less than 10% is excreted unchanged in the urine. About 70 - 80% of the dose is excreted with the urine in the form of the primary metabolite, a conjugate of 4-hydroxy-2,6-xylidine.

Pharmacokinetics in special patient groups
Given the rapid rate at which lidocaine is metabolised, the kinetics of lidocaine can be influenced by any condition that affects liver function. The half-life may increase by a factor of 2 or more in patients with hepatic disorders. Renal dysfunction has no influence on the kinetics of lidocaine but may lead to the accumulation of metabolites.

Children
Results from PK studies indicate that higher peak plasma levels are reached when lidocaine is applied topically on mucous membranes (nose, upper airways) to children aged between zero and three years when compared to older children and adults. Thus, children may be more sensitive to systemic effects due to increased blood levels of lidocaine.

The proposed medicinal product is not indicated for use in children below the age of 12 years.

IV.3 Pharmacodynamics
Pharmacotherapeutic group: local anaesthetic, ATC code: N01BB02

Primary pharmacology
Anaesthetic effect
The anaesthetic ingredient of Xylocaine 20mg/g Gel is Lidocaine, which stabilizes neuronal membranes and prevents the initiation and conduction of nerve impulses, thus effecting local anaesthetic action.

Lubricating effect
Xylocaine 20mg/g Gel is particularly indicated for anaesthesia of the urethra. The mucosa of a normal urethra is heavily folded. Thanks to the low surface tension and high viscosity of the solution, close and prolonged contact is created between the local anaesthetic and urethral mucosa; in men, even as far as the posterior part of the urethra. This provides complete anaesthesia of the entire urethra for 20-30 minutes. Hypromellose is considered to be the main ingredient of the medicinal product. Lubrication is known to reduce the vulnerability of sensitive tissues during catheterisation or introduction of instruments prior to procedures and is therefore considered to further support the local anaesthetic effect of the medicinal product.

Pharmacodynamic interactions with other medicinal products or substances
Potential for influence of lidocaine on the plasma levels/effect of other drugs
Lidocaine is metabolised by cytochrome P4501A2 (CYP1A2) and P4503A4 (CYP3A4); therefore, it has the potential to inhibit the metabolism of other drugs metabolised by these isoenzymes resulting in increased plasma levels of these products. To date, this has not been reported for any CYP1A2 or CYP3A substrate.

Amide-type local anaesthetics
Lidocaine should be used with caution in patients also using other local anaesthetics or other agents structurally related to amide-type local anaesthetics. Examples of these include antiarrhythmics such as mexiletine or tocainide. Since the systemic, toxic effects are additive, there is a risk of overdose.

Class III antiarrhythmics
There have been no specific interaction studies performed with lidocaine and class III antiarrhythmics (such as amiodarone), but caution must be exercised when treating patients.

CYP3A4 inducers
During concomitant administration with CYP3A4 inducers (e.g., carbamazepine, phenobarbitone, and phenytoin), decreased plasma levels of lidocaine have been reported. Primidone has also been reported to induce the metabolism of lidocaine.

Cimetidine or beta-blockers
If lidocaine is used repeatedly at high doses for a prolonged period, medicinal products that reduce the clearance of lidocaine, such as cimetidine or beta-blockers like metoprolol, nadolol, and propranolol, could theoretically lead to a clinically relevant increase in plasma levels. This is not to be expected with short-term use of Xylocaine 20mg/g Gel at the recommended dosage.

Methaemoglobinaemia
Methaemoglobinaemia may be accentuated in patients already taking methaemoglobin-inducing medicinal products (e.g. sulphonamides, nitrofurantoin, phenytoin, phenobarbital).

IV.4 Clinical Efficacy

The evaluation of the clinical efficacy of lidocaine hydrochloride monohydrate has been performed on a bibliographic basis. The applicant has provided evidence from several sources to support each of the proposed indications.

Adults

Efficacy of Xylocaine 20mg/g Gel in intraurethral procedures

The Clinical Overview reports that there are several uncontrolled studies describing the successful use of lidocaine gel for urethral procedures with both rigid and flexible endoscopes. These studies included more than 2,000 patients. In men, maximum dosage used was 40 ml (800 mg of lidocaine) and application time varied from 5 to 15 min. Also, after the application of gel in men, penile clamp was mostly used. In women, dosage of up to 5 ml was applied to the meatus either directly or with the help of cotton-tipped device.

Studies described above confirmed use of 20 ml of 2% lidocaine gel as anaesthetic and lubricant for urethral procedures in men, as lower volume may result in insufficient anaesthesia. Also, penile clamp should be used after application and application time should be 5-15 min. In women this can be lower, and 5-10 ml of the gel can be recommended, with application time of 5-10 min. Regarding the length of duration, in one study in men, duration of analgesia was found to be about 30 min. It was also confirmed that doses up to 40 ml (800 mg) of gel are within safe limits.

Efficacy of Xylocaine 20mg/g Gel in upper airways (nasal and pharyngeal cavities, and endotracheal intubation)

Studies confirmed that lidocaine gel can be used in the upper airways for procedures which require introduction of instruments or tubes into the nasopharynx and the respiratory tract. However, the dosage depends on the type of procedure, and maximal recommended volume should be 20 ml (400 mg of lidocaine). For procedures that do not require high volumes, such as endotracheal intubation, doses of 1-2 ml are sufficient.

Efficacy of Xylocaine 20mg/g Gel in rectal procedures

Studies have shown that up to 20 ml of 2% lidocaine gel can be used for anal and rectal procedures such as anal stretch. The total dose should not exceed 400 mg of lidocaine. However, documentation was not sufficient to support more prolonged use of gel. (Serpell MG et al 1993; Kumar CM et al 1988; Gough MJ et al 1983; Bjorck S et al 1992)

Adolescents aged 12 years and over:

Efficacy data are limited in this population however the Applicant provided adequate justification that the efficacy data in adults can be considered for adolescents as well based on EMA Reflection Paper on Extrapolation and ICH E11A. The paediatric extrapolation approach, together with the EU authorisation history, safety data and real-world experience are acknowledged and considered supportive of use in adolescents above 12 years.

Children under 12 years of age:

Efficacy data for lidocaine 2% gel in all indications are limited in this population.
The BNF for Children recommends a maximum dose of approximately 3 mg/kg for topical or mucosal lidocaine, and other authorised products recommend a dose of up to 2.9 mg/kg.

The proposed medicinal product is not indicated for use in children below the age of 12 years.

IV.5 Clinical Safety

The safety profile of lidocaine including topical lidocaine formulations, is well known. No new safety studies have been conducted by the applicant. The applicant evaluation of the clinical safety of lidocaine hydrochloride monohydrate has been performed on a bibliographic basis.

Adverse reactions

The following adverse reactions have been reported and are outlined in the SmPC.

General disorders and administration site conditions

Postoperative complaints of sore throat have been observed after the use of Xylocaine 20mg/g Gel for endotracheal intubation.

Immune system disorders

Hypersensitivity reactions - in the most severe cases, anaphylactic shock - as a result of local amide-type anaesthetics. Other components of Xylocaine 20mg/g Gel, e.g. methyl- and propyl p-hydroxybenzoate, can also cause similar reactions.

Injury, poisoning and procedural complications
Lidocaine may cause signs of acute toxicity if high plasma levels occur as a result of rapid absorption or overdose.

Contraindications
Contraindicated in patients with hypersensitivity to the active substance, excipients, amide-type local anaesthetics, such as bupivacaine, mepivacaine and prilocaine are proposed.
Given the potential risk of high systemic lidocaine levels and limited data on the efficacy in this age group and in line with the SmPCs of other similar products, use in children aged under 2 years is contraindicated.

Allergic reaction
Allergic reactions have been observed with the use of lidocaine gel. Feldman (1994) has shown that allergic reactions (in most severe instances anaphylactic shock) to local anaesthetics of amide type are rare (<1/1,000). The SmPC warns accordingly in section 4.8.

Excessive absorption
High dosages or short intervals between doses can lead to high plasma concentrations and, possibly, to serious adverse reactions. The absorption of lidocaine gel from the nasopharynx is variable but usually lower than with other lidocaine products (Efthimiou J et al; Scavone et al; Nydahl PA et al). Following instillation in urethra and bladder, adsorption is low. However, single cases had relatively high concentrations after application to urethra, but all these concentrations were below toxic levels.) Absorption from wound surfaces and mucous membranes is relatively high, especially in the bronchial tree. Administration in these areas may therefore lead to rapidly increasing or excessively high plasma concentrations, with an increased risk of toxic effects, such as convulsions. (Tucker et al 1988; Nydahl PA et al 1988; Kotaki H et al 1996; Axelsson K et al 1983; Efthimiou J et al 1982)

Application to damaged mucous membranes leads to increased systemic absorption. In adults, high plasma concentrations, up to 8 mg/l have been observed after the use of gel. The systemic uptake of lidocaine may be very fast and unpredictable when the dermal barrier is damaged as in burns (Wehner D et al, 1984). Following use of lidocaine gel on burns, convulsions have been described in case report of a child. The patient recovered with no apparent sequelae (Wehner and Hamilton, 1984). The SmPC warns accordingly in section 4.4.

Aspiration when applied to oropharyngeal area
Aspiration when applied to oropharyngeal area has been observed with the use of lidocaine gel (case reports). No relevant literature was found. The SmPC warns accordingly in section 4.4.

Methaemoglobinaemia
Cases of methaemoglobinaemia have been reported in association with local anaesthetic use. Patients with defective glucose-6-phosphate dehydrogenase, hereditary or idiopathic methaemoglobinemia are more susceptible to active-substance-induced signs of methaemoglobinaemia. In glucose-6-phosphate dehydrogenase deficient patients, the antidote methylene blue is ineffective at methaemoglobin reduction, and is capable of oxidising haemoglobin itself, and therefore methylene blue therapy cannot be given.
Methaemoglobinaemia may be accentuated in patients already taking methaemoglobin-inducing medicinal products (e.g. sulphonamides, nitrofurantoin, phenytoin, phenobarbital).
The SmPC warns accordingly in sections 4.4 and 4.5.

Porphyria
Sunesson-Palmgren concluded, based on decision of European Porphyria Initiative to use database published by Porphyria Centre Sweden and Norwegian Porphyria Centre as a platform for a European system of drug recommendations in the acute porphyries, that lidocaine is probably porphyrinogenic and should only be prescribed to patients with acute porphyria on strong or urgent indications. Appropriate precautions should be taken for all porphyric patients. The SmPC warns accordingly in section 4.4.

Overdose
Toxic reactions originate mainly in the central nervous system and the cardiovascular system (Feldman, 1994)

Central nervous system toxicity is a graded response, with symptoms and signs of escalating severity. The first symptoms are circumoral paraesthesia, numbness of the tongue, light-headedness, hyperacusis and tinnitus. Visual disturbance and muscular tremors are more serious and precede the onset of generalised convulsions. Unconsciousness and grand mal convulsions may follow, which may last from a few seconds to several minutes. Hypoxia and hypercarbia occur rapidly following convulsions due

to the increased muscular activity, together with the interference with normal respiration. In severe cases apnoea may occur. Acidosis increases the toxic effects of local anaesthetics.

Recovery is due to redistribution and metabolism of the local anaesthetic drug from the central nervous system. Recovery may be rapid unless large amounts of the drug have been administered.

Cardiovascular effects are only seen in cases with high systemic concentrations. Severe hypotension, bradycardia, arrhythmia and cardiovascular collapse may be the result in such cases.

Cardiovascular toxic effects are generally preceded by signs of toxicity in the central nervous system unless the patient is receiving a general anaesthetic or is heavily sedated with drugs such as a benzodiazepine or barbiturate.

Cardiac effects
Since local anaesthetics may have a suppressant effect on the heart, patients with partial or complete heart block should receive special attention before starting treatment with lidocaine.

Safety in special populations

Children under 12 years
Under 2 years: Given the potential risk of high systemic lidocaine levels and limited data on the efficacy in this age group and in line with the SmPCs of other similar products, use in children aged under 2 years is contraindicated.

Aged 2-12 years:
Safety data for lidocaine 2% gel in all indications are limited in this population.
The BNF for Children recommends a maximum dose of approximately 3 mg/kg for topical or mucosal lidocaine, and other authorised products recommend a maximum dose of 2.9 mg/kg for lidocaine hydrochloride that should not be exceeded in children aged 2 to 12 years.

As systemic absorption of lidocaine can be increased in children, caution is accordingly required to ensure that the recommended dose is not exceeded.

The proposed medicinal product is not indicated for use in children below the age of 12 years.

Renal/Hepatic impairment
Given the rapid rate at which lidocaine is metabolised, the kinetics of lidocaine can be influenced by any condition that affects liver function. The half-life may increase by a factor of 2 or more in patients with hepatic disorders. Renal dysfunction has no influence on the kinetics of lidocaine, but may lead to the accumulation of metabolites.
Accordingly, warnings are added to sections 4.2 and 4.4 of the SmPC.

Elderly
Debilitated or elderly patients, acutely ill patients or patients with sepsis should be given doses in accordance with their age, weight, and physical condition. The SmPC warns accordingly.

Pregnancy
Data on topical use of lidocaine during a large number of human pregnancies provide no indications of harmful effects. Lidocaine crosses the placenta but is only absorbed systemically to a limited extent when topically administered. The use of topical lidocaine may be considered during pregnancy, if clinically needed.

Lactation
Studies have shown that lidocaine is excreted in human milk. (Zeisler JA et al 1986)
Given the limited systemic absorption and hence very low exposure to lidocaine at therapeutic doses of Xylocaine 20mg/g Gel, no effects on breastfed newborns/infants are anticipated.

Fertility
Available literature information indicates that there is no specific human data is available on known effect of lidocaine on fertility. The SmPC informs accordingly.

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 Xylocaine 20mg/g Gel (Lidocaine hydrochloride 20mg).

Safety specification

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

Pharmacovigilance Plan
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Periodic Safety Update Report (PSUR)

With regard to PSUR submission, the MAH should take the following into account:

- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.
- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

IV.6 Discussion on the clinical aspects

This application is submitted based upon Article 10a of Directive 2001/83/EC. The bibliographic application demonstrates that lidocaine hydrochloride monohydrate has a well-established use, with an acceptable level of safety and efficacy for the proposed indications and posology, as outlined in Part II.1 of Annex I to Directive 2001/83/EC.

It has been demonstrated that the product or an equivalent product(s) has been in medicinal use for the proposed indication for at least 10 years with an acceptable level of efficacy and safety.

There was no discussion in the CMD(h). Based on the final positions of the CMSs and the discussions thereafter it is concluded that all concerned Member States are in agreement with the RMS.

V. OVERALL CONCLUSIONS

This application concerns an Article 10a of Directive 2001/83/EC, "well established use" for a Marketing Authorisation Application (MAA) for Xylocaine 20mg/g Gel (lidocaine hydrochloride monohydrate).

Given the status of well-established use, the applicant has not undertaken any new clinical trials with the Xylocaine 20mg/g Gel, and this is therefore a bibliographic application based on a comprehensive search of the published literature.

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

The HPRA, on the basis of the data submitted, considered that Xylocaine 20mg/g Gel demonstrated adequate evidence of efficacy for the approved indication(s) as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

VI. REVISION DATE

07.05.2031