

AMETHOCAINE



*“The Arnolfini Portrait”, Tempera on wood, 1434, Jan Van Eyck, National Gallery London*

*“...Bruges is a large and very wealthy city, and one of the greatest markets in the world. It is said that two cities compete with each other for commercial supremacy, Bruges in the West, and Venice in the East. It seems to me however, and many agree with my opinion, that there is much more commercial activity in Bruges. It offers everything that the whole world produces. I saw there oranges and lemons, fruits and wine from Greece, as abundant as in that country. I saw also confections and spices from Alexandria, and all the Levant, just as if one were there; furs from the Black Sea as if they had been produced in the district. Here was all Italy with its brocades, silks and armour, and everything which is made there; and indeed there is no part of the world whose products are not found here at their best”.*

*Petro Tafur, 1438.*

*The “Arnolfini Portrait”, is one of the most famous and enigmatic paintings in the National Gallery of London. Historians have long argued over the nature of its “true” message, or messages. Of one thing there is universal agreement. Jan Van Eyck provided for posterity a priceless and rare realistic glimpse into the home life of an upper middle class Renaissance couple. The early Fourteenth century saw the earliest signs of the Flemish and Dutch dominance over world trade and commerce that would finally surpass the age long Venetian hegemony. Historian Lisa Jardine, in her bestseller, “Worldly Goods”, sees the Van Eyck work as powerful evidence for her view that the Renaissance and its insatiable appetite for new learning sparked exploration of the High Seas which in turn created now found wealth and a consequent new appetite for the accumulation of “worldly goods”. The portrait shows a wealthy merchant, possibly a certain Italian, by the name of Arnolfini and his wife, or wife to be, Giovanna Cenami. Both are dressed in elaborate costumes. Arnolfini wears a sumptuous velvet cloak lined with expensive mink or possibly even Russian sable. He wears an elaborate velvet top hat. These were very popular and could reach monstrous proportions. Philip the Good, Duke of Burgundy introduced black and dark colours for formal and solemn occasions, as worn by Arnolfini. This fashion would later evolve into the hallmark black of Spanish Court dress in the Sixteenth century. The woman’s luxurious green gown is lined with ermine, and the elaborate folds of her train have been carefully arranged on the floorboards by a maid. The room is full of the spoils of trade, oriental rugs lie on the floor, and exotic oranges on the window-sill and the table underneath it. A lavish chandelier hangs overhead and an equally impressive glass mirror hangs on the far wall, a luxury possessed by only the very well to do. The bed and couch are covered with the richest quilts, Gothic carvings adorn the high backed chair.*

*In an age when most were illiterate, symbolism became extremely important in works of Art. Objects became words for the masses. Late medieval symbolism was extremely rich, but sadly much of its meaning is now lost to us in the 21st century. Some symbols are known to us however, such as the small dog, symbol of loyalty and fidelity, and the translucent rosary beads and flawless glass mirror, symbols of the purity of the bride. The clogs may seem out of place lying untidily on the floor, but to van Eyck’s contemporaries, they conveyed a clear message of “holy ground”. God spoke to Moses in the Old Testament, “Do not come any closer, take off your sandals, for you are standing on holy ground”.*

*The greatest controversy of the Arnolfini Portrait lies in the exact relationship between the couple. Is the work a celebration of a marriage, or a pregnancy, or even a memorial to a wife who died in childbirth? To the modern eye the woman certainly appears to be pregnant, with bulging stomach and hand held over it - which somewhat argues against the marriage theory! But some expert commentators, such as Rose-Marie and Rainer Hagen, have argued that no, she is not in fact pregnant. The woman merely portrays an attractively protruding female tummy, beloved of the Gothic Artistic tradition, and she merely holds up her long train from the ground. The Hagens argue that rather the image portrays a marriage. In the early Fifteenth century neither a priest nor a witness were required to enter into a legal Christian marriage! The mere pledge to each other was enough. And a wedding could be performed anywhere - even in a private bed chamber as depicted here. It would not be until the Council of Trent, over a century later that the Church decreed that attendance of a priest and two witnesses were necessary for a legal marriage to take place, and this was not so much for religious reasons as to clamp down on the abuse and deception that routinely occurred under the old system.*

*There is something else odd though about the portrait. Although witnesses were not required at the time the portrait on close inspection show that there are in fact two. They are seen reflected in the mirror! Why would it be necessary for witnesses? Some think that perhaps this was a morganatic marriage - that is one of unequal social rank, and legally which prevents the passage of the husband's titles and privileges to the wife and any children born of the marriage. Support for this theory lies in the details of the couple's hands. Conventionally the man took the woman's right hand in his right hand - a partnership of equals. But in this case, the wealthy man takes the woman's right hand in his left. The woman is beneath his social class. This is a marriage of unequal partnership. A legal contract will be required and so too will witnesses. Another fascinating clue lies in the highly unusual and elaborate way in which van Eyck signed his name to the painting. Conventionally this would appear modestly at one extreme corner of the work, but here it appears most elaborately, centrally and prominently on the far wall between the chandelier and the mirror. But there is still more to it than this. The inscription itself is highly unusual. Normally van Eyck's signature read "Johann de Eyck fecit hoc" (Jan van Eyck did this). Instead in the Arnolfini portrait it reads, "Johann de Eyck fuit hic" (Jan van Eyck was here) - that is he - "was a witness". The painting is more than a decorative item. It is a legal document! The great Spanish Artist Diego Velasquez famously depicted himself painting his subjects, via a mirror image view in his Las Meninas in 1656. It has been surmised that the man in blue, reflected in the mirror of the Arnolfini Portrait, is in fact the painter van Eyck himself. He bears witness to the marriage not only by his signature but also by his physical presence!*

*The famous Arnolfini Portrait shows us just how difficult it can be to ascertain for certain whether a woman is pregnant or not when this pregnancy is in the early stages. Is she pregnant? Or does she merely have an attractive "Gothic tummy"? In Gothic times this was an easy question to ask. However to ask this question in the 21st century may risk the dreaded social faux pas! We can relax however in the medical setting of applying anaesthetic drops to the eye. "I only ask, madam because it determines which drops I am to use - oxybuprocaine if you are not in early pregnancy, amethocaine if you are". Social faux pas nicely avoided!*

## AMETHOCAINE



*Amethocaine (or tetracaine) sterile drops 0.5 % (for single use)  
(Minims- Bausch & Lomb)*

### Introduction

**Amethocaine** (also known as **Tetracaine**) is a local anaesthetic agent formulated for:

- Topical use on the eye.
- Topical use on the skin.

**It is thought to be safer for use in pregnancy, than oxybuprocaine, particularly in the first trimester.**

It is useful for short painful procedures.

Amethocaine is on the **World Health Organization's** List of Essential Medicines, a list of the most important medication needed in a basic health system.

**See also separate document on Eye Drops Instillation (in Ophthalmology folder)**

### Classification

Topical local anaesthetic agents currently include:

1. Oxybuprocaine

2. **Amethocaine**
3. Lignocaine with fluorescein
4. Proxymetacaine

Oxybuprocaine is a local anesthetic of the **ester type**, (as opposed to the amide type).

### Chemistry

Amethocaine is a local anesthetic of the **ester type**, (as opposed to the amide type).

### Preparation

#### Liquid drops:

Amethocaine hydrochloride as:

- **Sterile, single use only solution in plastic dropper 0.5 ml solution.**

There are two strengths available:

- ♥ **0.5%**, (or **5 mg/mL**)
- ♥ **1%**, (or **10 mg/mL**)
- Preservative free, (preservative may affect microbiological culture).
- Topical ocular use only:
  - ♥ Amethocaine Eye Drops are for topical ophthalmic application only. This solution should *not* be injected.

#### Topical gel:

- **4 % gel**

#### Older topical preparations:

Amethocaine was a component of two older cutaneous preparations, now not generally used.

- EMLA:
  - ♥ The effect of amethocaine gel is generally *equivalent* to lignocaine with prilocaine (EMLA) but it is more **rapid in onset** and **longer lasting**.<sup>1</sup>

- ♥ EMLA is **non-sterile** and not approved for application to broken skin as there is insufficient data on absorption from these sites.<sup>4</sup>
- ALA (or Laceraine)
  - ♥ This is a combination of 0.3 agents: 5% amethocaine, 4% lignocaine and 0.1% adrenaline, which is **not** approved by the Therapeutic Goods Administration (TGA) but was nonetheless widely used in Australia for topical application.
  - ♥ Its maximum dose is 0.1 mL/kg.
  - ♥ The risk profile of ALA is similar to that of other local anaesthetics and, as with all these agents, careful attention must be paid to the total dose received by a patient as, in smaller children or those with larger wounds, inadvertent overdosing is a real risk.

### Mechanism of Action

Amethocaine acts like all other ester local anesthetic agents, by reversibly blocking fast sodium channels in nerve fibers.

### Pharmacodynamics

#### Ocular use

Onset of anaesthesia after instillation into the eye is 10 to 20 seconds.

Duration of anaesthesia is 10 to 20 minutes for the 0.5 % solution.

Duration of anaesthesia is up to 60 minutes for the 1 % solution.

#### Cutaneous use:<sup>4</sup>

Adequate anaesthesia usually occurs after:

- 30 minutes for venipuncture
- 45 minutes for venous cannulation

Anesthesia generally lasts for 4 - 6 hours after removal of the gel.

### Pharmacokinetics

#### Absorption:

- Most local anaesthetics, including amethocaine are readily absorbed through mucous membranes and through damaged skin.

- Amethocaine is also absorbed through intact skin.

#### Distribution:

- Local anaesthetics at tissue pH can diffuse through connective tissue and cellular membranes to reach the nerve fiber where ionization can occur.

#### Metabolism and excretion:

- The primary site of metabolism for amethocaine is the plasma.

Amethocaine is hydrolysed by plasma esterases (pseudocholinesterases) to para-amino benzoic acid and other metabolites and is excreted mainly by the kidneys.

Unmetabolised drug is excreted in the urine.

#### Indications

**Note that amethocaine is preferred over oxybuprocaine in pregnancy, particularly during the first trimester.**<sup>3</sup>

#### Ocular use

1. Short-term (< 20 minutes) ocular surface anaesthesia for simple procedures:
  - e.g. Removal of foreign bodies or minor surgery.
2. For immediate relief of severe ocular pain:
  - e.g. chemical burns, ultraviolet keratitis (flash burns)
3. To assist in ocular irrigation:
  - Including application of the Morgan Lens device.
4. For some forms of tonometry measurement:
  - e.g. Shoitz tonometry.

#### Cutaneous use:

Primarily used in children for:

1. Venipuncture
2. IV cannulation

3. Adjunct to lignocaine inflation for wound suturing

### Contra-indications/precautions

These include:

1. Known allergy to oxybuprocaine.
2. Prolonged or frequent use on the eye:
  - Frequent or chronic use may result in **severe corneal damage, keratitis and acquired tolerance.** <sup>2</sup>
3. Amethocaine is hydrolysed in the body to **p-amino benzoic acid** and should therefore not be used in patients being treated with **sulphonamides.** <sup>2</sup>

### Pregnancy

**Amethocaine** (and **proxymetacaine**) are classified as Australian category B2 drugs with respect to pregnancy.

The **RWH Pregnancy & Breastfeeding Guidelines** say the following: <sup>3</sup>

- Maternal use of **amethocaine** has not been associated with an increased risk of congenital malformations or adverse pregnancy outcomes.

Topical preparations of amethocaine are safe to use during pregnancy as systemic absorption is expected to be minimal. <sup>3</sup>

### Breast feeding:

The **RWH Pregnancy & Breastfeeding Guidelines** say the following:

- Published information describing the use of amethocaine during breastfeeding has not been located.
- Topical applications of amethocaine are safe to use during breastfeeding as systemic absorption is expected to be minimal.

### Adverse Effects

#### Ocular use:

1. Allergy (rare):
  - Remove the dermatological gel immediately if severe redness, swelling, itching or blistering occurs.

2. Some *mild* initial stinging sensation (30 seconds only):
  - **Proxymetacaine** may be preferred to amethocaine in **children** as it causes less stinging. <sup>4</sup>
3. Prolonged use can **impair corneal epithelial healing**.
  - Local anaesthetics are known to inhibit the rate of movement of corneal epithelial cells migrating to cover wounds. <sup>2</sup>
4. Prevents **reflex ocular protection** (from foreign bodies).
5. Can mask the progression of keratopathy.
6. Topical ocular anaesthetics can increase corneal permeability and so can increase the intraocular bioavailability of other topical drugs.

#### Topical use:

- Broken skin:
  - ♥ Do not apply; as there is an increased rate of absorption and so increased risk of adverse effects. <sup>1</sup>

#### Dosing

##### Ocular use:

##### Adult / child: <sup>1</sup>

- 1 drop, repeated in 5 minutes if necessary.
- Up to 3 doses may be used for foreign body removal or minor surgery
- Up to 5 doses for prolonged anaesthesia (eg cataract extraction).

**See also separate document for correct Eye Drops Instillation (in Ophthalmology folder)**

Topical ocular anaesthetics (although they may produce some **mild** initial stinging themselves) can reduce the (more significant stinging) initial stinging of some *other topical drugs* and so should be instilled first. <sup>1</sup>

Discard unused contents

The anaesthetized eye should be protected (i.e with an eye pad) from dust until anaesthesia has completely resolved.

Cutaneous use:<sup>4</sup>

Bring the gel to room temperature.

1 month - 18 years, apply a thick layer of gel the size of a \$2 coin (0.5 gram).

Do not spread or rub the gel in.

Cover with an occlusive dressing, leave for 30 - 60 minutes (maximum 60 minutes), then remove dressing *and* gel.



*"The Arnolfini Portrait", (Details) Tempera on wood, 1434, Jan Van Eyck, National Gallery London*

References

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2. Amethocaine Eye Drops in MIMs Website, 1 October 2010.
3. Amethocaine in RWH Pregnancy & Breastfeeding Guidelines; 17 February 2015.
4. Amethocaine Dermal in Australian Medicines Handbook for Children Website, Accessed November 2015.
5. Benjamin Lawton, Andrew Hadj. Laceration repair in children. Aust Fam Phys. Vol 43, no. 9. September 2014.

Dr J. Hayes.  
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