# PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

## SCHEDULING STATUS

S5

## 1 NAME OF MEDICINE

QUIFOL 1 %w/v Injection

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of QUIFOL 20 ml contains 10 mg/ml of propofol.

Sugar free

For the full list of excipients, (see section 6. 1)

QUIFOL 20 ml contains soya oil. If you are allergic to peanut or soya, do not use this medicinal product. the threshold for this excipient is zero.

## 3 PHARMACEUTICAL FORM

Injection (inj.)

A white or almost white, homogenous emulsion, practically free from extraneous particulate contamination and large oil droplets. Slight creaming may be visible on prolonged standing.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indication

a) Induction and maintenance of general anaesthesia as part of a balanced anaesthetic technique.

b) Sedation of ventilated adult patients receiving intensive care, for a period of up to 72 hours.

c) Conscious sedation for surgical and diagnostic procedures in adults provided that there are adequate facilities for monitoring of haemodynamic and oxygenation parameters and if administered by a qualified anaesthetist.

## 4.2 Posology and method of administration

### Posology

Supplementary analgesic medicines are required in addition to QUIFOL, where analgesia is required.

QUIFOL has been used in association with spinal and epidural anaesthesia and with commonly used premedication, neuromuscular blocking medicines, inhalation and analgesic medicines; no pharmacological incompatibility has been encountered.

Dosage adjustment may be necessary when used together with the above medicines, particularly the narcotics (e.g. morphine, meperidine and fentanyl), combinations of opioids and sedatives (e.g. benzodiazepines, barbiturates, droperidol etc.), supplementary analgesic medicines (e.g nitrous oxide or opioids) and the potent inhalation medicines (e.g. isoflurane, enflurane and halothane).

Where general anaesthesia with QUIFOL is used simultaneously with a regional anaesthetic technique, lower doses of QUIFOL may be required.

When QUIFOL is used undiluted to maintain anaesthesia, it is recommended that equipment such as drop counters, syringe pumps or volumetric infusion pumps should always be used to control infusion rates. QUIFOL can be used for infusion undiluted from glass infusion bottles, or plastic syringes. QUIFOL can be diluted with 5 % dextrose intravenous infusion only, in PVC infusion bags or glass infusion bottles. Dilutions, which must not exceed 1 in 5 (2 mg propofol

per ml) should be prepared aseptically immediately before administration and must be used within 6 hours of preparation.

The dilution may be used with a variety of infusion control techniques but a giving set used alone will not avoid the risk of accidental, uncontrolled infusion of large volumes of diluted QUIFOL. A burette, drop counter or volumetric pump must be included in the infusion line. The risk of uncontrolled infusion must be taken into account when deciding the maximum amount of QUIFOL in the burette.

It is recommended that, when using diluted QUIFOL, the volume of 5 % dextrose removed from the infusion bag during the dilution process is totally replaced in volume by QUIFOL emulsion.

QUIFOL may be administered via a Y-piece close to the injection site, into intravenous infusions of dextrose 5 % or sodium chloride 0.9 %.

QUIFOL may be premixed with alfentanil injection.

In order to reduce pain on initial injection, that part of the QUIFOL used for induction may be mixed with lignocaine injection in the ratio of 20 parts QUIFOL with up to 1 part of 1 % lignocaine injection immediately prior to administration.

It is recommended that blood lipid levels be monitored routinely should QUIFOL be administered to patients thought to be at particular risk of fat overload. Administration of QUIFOL should be adjusted appropriately if the monitoring indicates that fat is being inadequately cleared from the body. If the patient is receiving other intravenous lipid concurrently, a reduction in quantity should be made in order to take account of the amount of lipid infused as part of the QUIFOL formulation; 1,0 ml of QUIFOL contains 0,1 g of fat.

Patients with hypovolaemia should have fluid-volume deficits corrected prior to administration of QUIFOL.

**Method of Administration**

For intravenous administration

ADULTS

Induction of general anaesthesia:

QUIFOL may be used to induce anaesthesia by slow bolus injection or infusion.

In unpremedicated and premedicated patients:

Most adult patients aged less than 55 years are likely to require 1,5 to 2,5 mg/kg (0,15 to 0,25 ml/kg) of QUIFOL, (approximately 4 ml every 10 seconds in an average healthy adult) by slow bolus injection or infusion titrated against the response of the patient until clinical signs show onset of anaesthesia. The total dose required can be reduced by lower rates of administration (20 to 50 mg/min [2 to 5 ml/min]).

Over the age of 55 years the requirement will generally be less. In patients of ASA Grades 3 and 4, lower rates of administration should be used (approximately 20 mg [2 ml] every 10 seconds).

Maintenance of general anaesthesia:

Anaesthesia can be maintained by administering QUIFOL either by continuous infusion or by repeat bolus injections to prevent the clinical signs of light anaesthesia.

Infusion:

The average rate of administration varies between patients, but rates in the region of 4 to12 mg/kg/hr (0,4 to1,2 ml/kg/hr) usually maintain satisfactory anaesthesia.

Slightly higher rates of administration may be required for 10 to 20 minutes after induction of anaesthesia.

Repeat bolus injections:

As a guide, increments of 25 mg (2,5 ml) to 50 mg (5,0 ml) may be used.

Sedation during intensive care:

To provide sedation for ventilated adult patients undergoing intensive care, it is recommended that QUIFOL be given by continuous infusion, for up to 72 hours. Adjust infusion rate according to the depth of sedation required. Rates of 0,3 mg/kg/hr to 4,0 mg/kg/hr should achieve satisfactory sedation. Rates above 4,0 mg/kg/hr are not recommended.

Conscious sedation for surgical and diagnostic procedures (section 4.4):

To provide sedation for surgical and diagnostic procedures rates of administration should be individualised and titrated to clinical response.

Most patients will require 0.5 mg/kg to 1 mg/kg over 1 to 5 minutes to initiate sedation.

Maintenance of sedation may be accomplished by titrating QUIFOL infusion to the desired level of sedation - most patients will require 1.5 mg/kg/hr to 4.5 mg/kg/hr. In addition to the infusion, bolus administration of 10 mg to 20 mg may be used if a rapid increase in the depth of sedation is required. In patients in ASA Grades 3 and 4 the rate of administration and dosage may need to be reduced.

ELDERLY PATIENTS

In elderly patients the dose requirement for induction of anaesthesia with QUIFOL is reduced. The reduction should take account of the physical status and age of the patient. The reduced dose should be given at a slower rate and titrated against the response.

Where QUIFOL is used for maintenance of anaesthesia or sedation the rate of infusion or “target concentration” should also be reduced. Patients of ASA Grades 3 and 4 will require further reductions in dose and dose rate. Rapid bolus administration (single or repeated) should not be used in the elderly as this may lead to cardio respiratory depression.

CHILDREN

Induction of general anaesthesia:

QUIFOL is not recommended for use in children less than 3 years of age (see section 4.3).

It is recommended that QUIFOL be given slowly until the clinical signs show the onset of anaesthesia. Adjust dose for age and/or mass. Most patients over 8 years of age are likely to require approximately 2.5 mg/kg (0.25 ml/kg) of QUIFOL for induction. Under this age the requirement may be more. Lower dosage is recommended for children of ASA Grades 3 and 4.

Maintenance of general anaesthesia:

QUIFOL is not recommended for use in children less than 3 years of age.

Administer QUIFOL by infusion or repeat bolus injection to maintain the depth of anaesthesia required. The required rate of administration varies considerably between patients. 9 mg/kg/hr to 15 mg/kg/hr (0.9 ml/kg/hr to 1.5 ml/kg/hr) usually achieves satisfactory anaesthesia.

Conscious sedation for surgical and diagnostic procedures:

QUIFOL is not recommended for conscious sedation in children as safety and efficacy have not been demonstrated.

Sedation during intensive care:

QUIFOL is not recommended for sedation in children as safety and efficacy have not been demonstrated. Although no causal relationship has been established, serious adverse events (including fatalities) have been observed from spontaneous reports of unlicensed use and these events were seen most often in children with respiratory tract infections, given doses in excess of those recommended for adults.

Associated findings include metabolic acidosis, lipaemia, rhabdomyolysis, cardiac irregularities and renal failure.

### 4.3 Contraindications

QUIFOL is contraindicated in:

- Known hypersensitivity to the active substance propofol or to any of the excipients listed in section 6.1.
- QUIFOL is not recommended in children under the age of 3 years.
- Sedation of children of all ages with croup or epiglottitis receiving intensive care (see Section 4.4).
- Appropriate care should be applied in patients with disorders of fat metabolism, patients predisposed to fat embolism and in other conditions where lipid emulsions must be used cautiously.
- Fat metabolism may be disturbed in conditions such as renal insufficiency, uncompensated diabetes mellitus, certain forms of liver insufficiency, metabolic disorders, severe trauma including long-bone and multiple fractures, and sepsis.

### 4.4 Special warnings and precautions for use

- Respiration will be depressed and must be monitored to ensure adequate gas exchange. Special care should be exercised when used with other respiratory depressants. Patients should be constantly monitored and facilities for maintenance of a patent airway, artificial ventilation and oxygen enrichment and other resuscitative facilities should be readily available at all times. QUIFOL should not be administered by the person conducting the diagnostic or surgical procedure.
- A generalised systemic reaction which may be anaphylactic in nature (including angioedema, bronchospasm, erythema and hypotension) may occur following QUIFOL administration - estimated as 1 in 15 000.
- When QUIFOL is administered to an epileptic patient, there may be a risk of convulsion.

- In the elderly, debilitated or ASA Grades 3 or 4 patients, rapid single or repeated bolus administration should not be used in order to minimise undesirable cardiorespiratory side effects.
- QUIFOL should be given by those trained in anaesthesia (or where appropriate, doctors trained in the care of patients in intensive care).

When QUIFOL is administered for conscious sedation, for surgical and diagnostic procedures, patients should be continually monitored for early signs of hypotension, airway obstruction and oxygen desaturation.

An adequate period is needed prior to discharge of the patient to ensure full recovery after general anaesthesia. Very rarely the use of QUIFOL may be associated with the development of a period of post-operative unconsciousness, which may be accompanied by an increase in muscle tone. This may or may not be preceded by a period of wakefulness. Although recovery is spontaneous, appropriate care of an unconscious patient should be administered.

Caution should be applied in patients with cardiac, respiratory, renal or hepatic impairment or in hypovolaemic or debilitated patients. The pharmacokinetics of propofol may be prolonged in people with chronic hepatic cirrhosis or chronic renal impairment. Recovery times may double as a result. The effects of acute hepatic or renal failure on the pharmacokinetics of propofol have not been studied.

EDTA is a chelator of metal ions, including zinc. The need for supplemental zinc should be considered during prolonged administration of QUIFOL, particularly in patients who are predisposed to zinc deficiency, such as those with burns, diarrhoea and/or major sepsis.

QUIFOL lacks vagolytic activity and has been associated with reports of bradycardia, occasionally profound and also asystole. The intravenous administration of an anticholinergic medicine before induction, or during maintenance of anaesthesia should be considered, especially in situations where vagal tone is likely to predominate or when QUIFOL is used in conjunction with other medicines likely to cause a bradycardia.

QUIFOL contains soya oil. If you are allergic to peanut or soya, do not use this medicinal product.

**4.5 Interaction with other medicines and other forms of interaction**

The neuromuscular blocking medicines, atracurium and mivacurium should not be given through the same intravenous line as QUIFOL without prior flushing.

QUIFOL has been used in association with spinal and epidural anaesthesia and with commonly used premedication, neuromuscular blocking medicines, inhalation and analgesic medicines; no pharmacological incompatibility has been encountered. Dosage adjustment may be necessary when used together with the above medicines, particularly the narcotics (e.g. morphine, meperidine and fentanyl), combinations of opioids and sedatives (e.g. benzodiazepines, barbiturates, droperidol etc.), supplementary analgesic medicines (e.g. nitrous oxide or opioids) and the potent inhalation medicines (e.g. isoflurane, enflurane and halothane).

Where general anaesthesia with QUIFOL is used simultaneously with a regional anaesthetic technique, lower doses of QUIFOL may be required.

**4.6 Fertility, pregnancy and lactation**

**Women of childbearing potential**

*Pregnancy:*

QUIFOL should not be used in pregnancy. QUIFOL crosses the placenta and may be associated with neonatal depression. It should not be used for obstetric anaesthesia. QUIFOL has been used, however, during termination of pregnancy in the first trimester.

*Breastfeeding*

In mothers who are breastfeeding, safety to the neonate has not been established.

Fertility

No data available.

### 4.7 Effects on ability to drive and use machines

Patients should be advised that performance at skilled tasks, such as driving and operating machinery, may be impaired for some time after general anaesthesia.

### 4.8 Undesirable effects

a) *Tabulated list of adverse reactions*

| **System organ class** | **Frequent** | **Less frequent** | **Frequency unknown** [(9)] |
|---|---|---|---|
| **Immune system disorders** | | Anaphylaxis - may include angioedema, bronchospasm, erythema, hypotension | |
| **Metabolism and nutrition disorders** | | | Metabolic acidosis[(5)], hyperkalaemia[(5)] hyperlipidaemia[(5)] |
| **Psychiatric disorders** | | | Euphoric moods, drug abuse and drug dependence[(8)] |
| **Nervous system** | Headache during recovery | Epileptiform movements, | Involuntary movement |

| | | | |
|---|---|---|---|
| **disorders** | phase, | including convulsions and opisthotonus during induction, maintenance and recovery postoperative unconsciousness | |
| **Cardiac disorders** | Bradycardia [1] | | Cardiac arrhythmia [5], cardiac failure [5][7] |
| **Vascular disorders** | Flushing in children[11], hypotension [2] | Phlebitis, thrombosis | |
| **Respiratory, thoracic and mediastinal disorders** | Transient apnoea during induction | Pulmonary oedema | Respiratory depression (dose dependent) |
| **Gastrointestinal disorders** | Nausea and vomiting during recovery phase | Pancreatitis | |
| **Hepatobiliary disorders** | | | Hepatomegaly [5] |
| **Musculoskeletal, connective** | | | Dystonia/dyskinesia Rhabdomyolysis |

| | | | |
|---|---|---|---|
| **tissue and bone disorder** | | | (3)(5) |
| **Renal and urinary disorders** | | Urine discolouration following prolonged administration | Renal failure (5) |
| **Reproductive system and breast disorders** | | Sexual disinhibition | Priapism |
| **General disorders and administration site conditions** | Local pain on induction (4) Withdrawal symptoms in children(11) | Tissue necrosis (10) following accidental extravascular administration | Local pain, swelling following accidental extravascular administration |
| **Investigations** | | | Brugada type ECG (5), (6) |
| **Injury and poisoning** | | Postoperative fever | |

1. Serious bradycardias are rare. There have been isolated reports of progression to asystole.
2. Occasionally, hypotension may require use of intravenous fluids and reduction of the administration rate of QUIFOL.
3. Very rare reports of rhabdomyolysis have been received where QUIFOL has been given at doses greater than 4 mg/kg/hr for ICU sedation.

4. May be minimised by using the larger veins of the forearm and antecubital fossa.
5. Combinations of these events, reported as “Propofol Infusion Syndrome”, may be seen in seriously ill patients who often have multiple risk factors for the development of the events.
6. Brugada-type ECG - elevated ST-segment and coved T-wave in ECG.
7. Rapidly progressive cardiac failure (in some cases with fatal outcome) in adults. The cardiac failure in such cases was usually unresponsive to inotropic supportive treatment.
8. Abuse of and drug dependence on propofol, predominantly by healthcare professionals.
9. Not known as it cannot be estimated from the available clinical trial data.
10. Necrosis has been reported where tissue viability has been impaired.
11. Following abrupt discontinuation of QUIFOL during intensive care.

*General:*

Side effects include excitation, involuntary movement, hiccup, flushing and hypertension.

During induction and maintenance of anaesthesia, hypotension and apnoea may occur. Hypotension may require use of intravenous fluids and reduction of the rate ofadministration of QUIFOL during the period of anaesthetic maintenance.

Less frequently, tachycardia, premature ventricular contractions, premature atrial contractions, syncope, abnormal ECG, and ST segment depression may occur.

Epileptiform movements, including convulsions and opisthotonos have been reported in 0.5 % at induction of anaesthesia, during maintenance of anaesthesia and during recovery. During the recovery phase nausea, vomiting and headache may occur.

There have been reports of rhabdomyolysis when QUIFOL has been administered at doses greater than 4 mg/kg/hr for ICU sedation.

Sexual disinhibition has been reported during recovery.

Pulmonary oedema.

Discolouration of urine has been reported following prolonged administration of QUIFOL.

There have been reports of post-operative fever.

Pancreatitis has been observed following the use of QUIFOL; a causal relationship has not been clearly established.

*Local:*

The local pain which may occur during the induction phase of QUIFOL anaesthesia can be minimised by the co-administration of lignocaine (see section 4.2) and by the use of the larger veins of the forearm and antecubital fossa.

Thrombosis and phlebitis may occur less frequently. Accidental clinical extravasation and animal studies showed minimal tissue reaction.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

**4.9 Overdose**

**Symptoms**

Accidental overdosage is likely to cause cardio respiratory depression.

**Treatment**

Respiratory depression should be treated by artificial ventilation with oxygen. Cardiovascular depression would require lowering of the patient's head, and, if severe, use of plasma expanders and pressor medicines.

## 5. PHARMACOLOGICAL

### 5.1 Pharmacodynamic properties

pharmacological classification: GABA receptor agonist; sedative; hypnotic

Pharmacotherapeutic group: non-barbiturate sedative

ATC code: N01AX10

Propofol Injection 1%w/v (2,6-diisopropylphenol) is a short-acting sedative hypnotic with a rapid onset of action of approximately 30 seconds.

The mechanism of action is poorly understood.

Falls in mean arterial blood pressure and changes in heart rate are observed when Propofol Injection 1%w/v is administered.

Ventilatory depression can occur following administration of Propofol Injection 1%w/v.

Propofol Injection 1%w/v reduces cerebral blood flow, intracranial pressure and cerebral metabolism.

Recovery from anaesthesia is usually rapid and clear-headed. Propofol Injection 1%w/v has an anti-emetic effect. Studies have shown that Propofol Injection 1%w/v, at the concentrations likely to occur clinically, does not inhibit the synthesis of adrenocortical hormones.

### 5.2 Pharmacokinetic properties

The decline in propofol concentrations following a bolus dose or following the termination of an infusion can be described by a 3-compartment open model. The first phase is characterised by a rapid distribution (half-life: 2 to 4 minutes) followed by rapid elimination (half-life: 30 to 60 minutes) and a slower final phase, representative of redistribution of propofol from poorly perfused tissue.

Propofol is extensively distributed and rapidly cleared from the body (total body clearance: 1,5 to 2 litres/minute). Clearance occurs by metabolic processes, mainly in the liver, to form inactive conjugates of propofol and its corresponding quinol, which are excreted in the urine.

The pharmacokinetics are linear over the recommended range of infusion rates of QUIFOL.

Under the usual maintenance regimens, significant accumulation of propofol does not occur.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Sodium oleate,

glycerin,

egg lecithin,

soyabean oil,

sodium hydroxide,

water for injection

### 6.2 Incompatibilities

Incompatibilities:

QUIFOL should not be mixed prior to administration with injections or infusion fluids other than 5 % dextrose or lignocaine injection or alfentanil injection (see above).

The neuromuscular blocking medicines, atracurium and mivacurium should not be given through the same intravenous line as QUIFOL without prior flushing.

### 6.3 Shelf life

36 months

### 6.4 Special precautions for storage

Store at or below 30 °C. Do not freeze or refrigerate.

Keep in the original packaging until required for use.

### 6.5 Nature and contents of container

The emulsion is presented in 20 ml glass vial The product is packed in 20 ml clear colorless glass vial USP type II closed with gray bromobutyl rubber stopper followed by pink coloured plastic flip off seal along with insert. 10 such monocarton are packed in a mother carton.

### 6.6 Special precautions for disposal and other handling

Propofol should only be mixed with the following products:

Propofol is compatible with Glucose Intravenous Infusion 5%, Dextrose 5% in Lactate Ringers solution, Sodium chloride 0.9% w/v intravenous infusion, and Dextrose 4% with 0.18% sodium chloride intravenous infusion for 8 hour at room temperature.

Any unused product or waste material should be disposed of in accordance with local requirements.'

In use precautions: General:

Containers should be shaken before use. QUIFOL should be inspected for particulate matter and discolouration before administration. Do not use if there is evidence of separation of the phases of the emulsion.

QUIFOL contains no antimicrobial preservatives and the vehicle supports growth of micro-organisms.

When QUIFOL is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after opening the ampoule or breaking the vial seal. Administration must commence without delay.

Asepsis must be maintained for both QUIFOL and infusion equipment throughout the infusion period. Any infusion fluids added to the QUIFOL line must be administered close to the cannula site. QUIFOL must not be administered via a microbiological filter.

Any container or syringe containing QUIFOL is for single use in a single patient only.

General anaesthesia:

In accordance with established guidelines for other lipid emulsions a single infusion of QUIFOL must not exceed 6 hours. The syringe or giving set and any unused portion of QUIFOL or solution containing QUIFOL must be discarded at the end of the surgical procedure, or at 6 hours, whichever is the sooner, and replaced as appropriate.

Intensive care sedation:

Administration should commence promptly and must be completed within 12 hours after the vial has been spiked. The tubing and any unused portions of QUIFOL must be discarded after 12 hours.

If QUIFOL is transferred to another container prior to administration, the handling procedures for “General anaesthesia” (above) should be followed and the product should be discarded and administration lines changed after 6 hours.

## 7 HOLDER OF CERTIFICATE OF REGISTRATION:

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## 8. REGISTRATION NUMBER:

56/2.1/1074

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22-July-2025

## 10. DATE OF REVISION OF THE TEXT

Not yet revised

QUIFOL is manufactured by

Aculife Healthcare Private Limited.

Unit 5, IPD, Village: Sachana,

Taluka: Viramgam,

District: Ahmedabad – 382150,

Gujarat, India.