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*To all Doctors and Nurses*

Blessings to all!

We at Medic-Pro Corp, an ISO 13485:2016 certified medical device manufacturer in the Philippines, would like to inform all health Professionals from government and private hospitals that our company strictly follows international standard, **ISO 13485 of (8536-4), that requires all infusion and transfusion sets to have a safety feature for the protection of the patients.**

This safety feature that **MUST** be present in all sets should have a **15 micron in-line filter** that will **prevent entry of foreign particles and air bubbles** into the blood circulation which will be a health risk and may even cause death to your patients.

ISO 8536-4 has been mandatory since 2007 in British and European communities and we must all work hand in hand so that the Philippines will soon follow and see the advantage it gives.

We must be vigilant in the selection of sets and this will make your reputable hospital known to promoting and extending excellent health services by which your community will be proud of.

Please see attached researches for your reference:

- *Drug to be Used with a Filter for Preparation and/or Administration*
  Reference: Hospital Pharmacy, Volume 42, Number 4, pp378-382 2007 Wolters Kluwer Health, Inc.
- *The Use of Integral Fluid Filters in Single-Use Infusion Administration Set*
  By: Joana Ford (R&D Officer, SMTL) and Pete Philips (Director, SMTL), November 2008

We hope to discuss more about our Infusion Sets with you and would like to request for a courtesy visit anytime at your convenience.

We look forward for a fruitful business relationship with your prestigious institution in the near future.

Thank you very much and more power!

**R&D**


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**Hospital Pharmacy**
Volume 42, Number 4, pp 378–382
2007 Wolters Kluwer Health, Inc.

# Special Resource

# Drugs to be Used with a Filter for Preparation and/or Administration

*Prepared by:* **Wolters Kluwer Health/Facts and Comparisons**
*Date:* **March 9, 2007**
*Disclaimer:* While every effort has been made to ensure the accuracy and completeness of the information presented in this chart, the reader is advised that the authors or Wolters Kluwer Health cannot be responsible for the currency of the information, for any errors or omissions, or for any consequences that may arise. The reader should consult the product package insert for the most up-to-date information.

## Drugs that Require a Filter

| Drug | Class | Filter Size[a] | Comments |
|---|---|---|---|
| Abatacept (*Orencia*) | Immunomodulator | 0.2 to 1.2 micron | Administer with an infusion set and a sterile nonpyrogenic, low-protein-binding filter. |
| Abciximab (*ReoPro*) | Glycoprotein IIb/IIIa inhibitor | 0.2 or 0.22 micron | For a bolus injection, filter prior to administration; for continuous infusion, filter either upon admixture (using a sterile, nonpyrogenic, low-protein-binding filter) or upon administration (using an inline, sterile, nonpyrogenic, low-protein-binding filter). |
| Agalsidase beta (*Fabrazyme*) | Enzyme | 0.2 micron | Do not use filter needles during the preparation of the infusion; diluted solution should be filtered through an inline low-protein-binding filter during administration. |
| Alglucosidase alfa (*Myozyme*) | Enzyme | 0.2 micron | Do not use filter needles during the preparation of the infusion; diluted solution should be filtered through an inline low-protein-binding filter during administration. |
| Alpha-1 proteinase inhibitor (eg, *Prolastin, Aralast, Zemaira*) | Respiratory enzyme | See individual package inserts | |
| Amiodarone (*Cordarone*) | Antiarrhythmic agent | Not specified | Use a 0.2 micron inline filter during administration; recommended by manufacturer. Another source suggests no significant loss of drug potency with the use of a 0.22 micron cellulose ester membrane filter.[1,2] |
| Amphotericin B desoxycholate (*Amphocin, Fungizone*) | Antifungal agent | 1 micron or larger mean pore diameter (inline membrane filter) | Filter may be used during administration. |
| Antihemophilic factor (eg, *Adurate, Kogenate*) | Antihemophilic agent | Not specified | Use filtered needle provided by manufacturer. |
| Antihemophilic factor/von Willebrand Factor Complex (*Humate P*) | Antihemophilic factor combination | Not specified | Use filter for withdrawal from the vial. |

*(continued)*

## Drugs that Require a Filter

| Drug | Class | Filter Size[a] | Comments |
|---|---|---|---|
| Antithymocyte globulin (*Thymoglobulin*) | Immune globulin | 0.22 micron inline filter | |
| Antithrombin III (*Thrombate III*) | Antithrombin agent | Not specified | Use filter needle provided by manufacturer. |
| Asparaginase (*Elspar*) | Antineoplastic agent | 5 micron | Filter during intravenous (IV) administration. |
| Botulism immune globulin IV (*BabyBIG*) | Immune globulin | 18 micron | Use inline or syringe-tip sterile, disposable filter. |
| Busulfan (*Busulfex*) | Antineoplastic agent | 5 micron | Do not use polycarbonate syringes or polycarbonate filter needles with busulfan; only use the 5 micron nylon[1] filter needle provided; use one filter per ampule. |
| Cetuximab (*Erbitux*) | Monoclonal antibody | 0.22 micron inline filter | |
| Citric acid, gluconodelta-lactone, and magnesium carbonate (*Renacidin*) | Urinary irrigant | Not specified | After thorough mixing, filter the solution through a coarse filter. |
| Cladribine (*Leustatin*) | Antineoplastic agent | 0.22 micron | When preparing the 7-day infusion solution, both cladribine and the diluent should be passed through a sterile disposable hydrophilic syringe filter as each solution is being introduced into the infusion reservoir. |
| Clofarabine (*Clolar*) | Antineoplastic agent | 0.2 micron | Filter prior to dilution. |
| Cytomegalovirus immune globulin IV, human (*CytoGam*) | Immune globulin | 15 micron inline filter | A 0.2 micron filter is also acceptable. |
| Digoxin immune Fab (*Digibind*) | Detoxification agent | 0.22 micron membrane filter | |
| Epoprostenol sodium (*Flolan*) | Vasodilator | 0.22 micron | An inline filter was used during clinical trials. |
| Ferumoxides (*Feridex IV*) | Diagnostic agents | 5 micron | |
| Galsulfase (*Naglazyme*) | Enzyme | 0.2 micron | Do not use a filter during preparation of the solution; administer with a polyvinyl chloride (PVC) infusion set equipped with an inline, low-protein-binding filter. |
| Gemtuzumab ozogamicin (*Mylotarg*) | Monoclonal antibody | 1.2 micron terminal filter | Can be given through central or peripheral line; administer through a separate line equipped with a low-protein-binding, 0.2 to 1.2 micron terminal filter; manufacturer states: The following filter membranes are qualified: 0.22 or 1.2 micron polyether sulfone (PES) *Supor*; 1.2 micron acrylic copolymer hydrophilic filter (*Versapor*); 0.8 micron cellulose mixed ester (acetate and nitrate) membrane; 0.2 micron cellulose acetate membrane.[1] |
| Hemin (*Panhematin*) | Hemin agent | 0.45 micron or smaller terminal filter | |

*(continued)*

## Drugs that Require a Filter

| Drug | Class | Filter Size[a] | Comments |
|---|---|---|---|
| Hyaluronidase powder for injection (*Vitrase*) | Enzyme | 5 micron | Use a filter needle when withdrawing the reconstituted solution from the vial. |
| Idursulfase (*Elaprase*) | Enzyme | 0.2 micron | Filter to be used with an infusion set. |
| Imiglucerase (*Cerezyme*) | Enzyme | 0.2 micron | Diluted solution may be filtered through an inline, low-protein-binding filter during administration. |
| Immune globulin IV (eg, *Gammagard, Flebogamma*) | Immune globulin | See individual package inserts | |
| In-111 ibritumomab tiuxetan and Y-90 ibritumomab tiuxetan (*Zevalin*) | Radioimmunotherapeutic monoclonal antibody | 0.22 micron | A low-protein-binding filter should be inline between the syringe and infusion port prior to injection of each component. |
| Infliximab (*Remicade*) | Monoclonal antibody | 1.2 micron or smaller inline filter | |
| Inulin | Diagnostic agent | Not specified | Administer through a filter. |
| Itraconazole (*Sporanox*) | Antifungal agent | Not specified | Use infusion set with filter provided by the manufacturer. |
| Lansoprazole (*Prevacid IV*) | Proton pump inhibitor | 1.2 micron | Administer using inline filter provided. |
| Laronidase (*Aldurazyme*) | Enzyme | 0.2 micron | Do not use a filter during preparation of the solution; administer with a PVC infusion set equipped with an inline, low-protein-binding filter. |
| Lymphocyte immune globulin, antithymocyte globulin (*Atgam*) | Immune globulin | 0.2 to 1 micron | |
| Mafenide (*Sulfamylon*) | Topical burn preparation | 0.22 micron | Filter reconstituted solution prior to use; topical use only. |
| Mannitol | Osmotic diuretic | 5 micron inline filter | To be used when infusing concentrated mannitol (20% or more). |
| Methacholine (*Provocholine*) | Diagnostic agent | 0.22 micron | A sterile, bacterial-retentive filter should be used when transferring a solution from each vial (at least 2 mL) to a nebulizer; initial use only. |
| Morphine sulfate soluble tablets for injection | Opioid | 0.22 micron | Prepare soluble tablets in sterile water and filter prior to administration. |
| Morphine sulfate for intrathecal administration (*Infumorph*) | Opioid | 5 micron or smaller | Filter through a microfilter before injecting into the microinfusion device; intrathecal use only. |
| Muromonab-CD3 (*Orthoclone OKT3*) | Monoclonal antibody | 0.2 or 0.22 micron | Draw solution into a syringe through a low-protein-binding filter. |
| Paclitaxel (*Taxol, Onxol*) | Antineoplastic agent | 0.22 micron or smaller | Administer through an inline filter; use of a filter is not recommended for *Abraxane*. |
| Panitumumab (*Vectibix*) | Monoclonal antibody | 0.2 or 0.22 micron | Administer by an IV infusion pump using a low-protein-binding inline filter. |

*(continued)*

## Drugs that Require a Filter

| Drug | Class | Filter Size[a] | Comments |
|---|---|---|---|
| Pentetate calcium trisodium | Detoxification agent | Not specified | May be filtered using a sterile filter if particles are seen subsequent to opening of the ampule. |
| Phenytoin sodium, parenteral | Anticonvulsant | Not specified (inline filter) | Although not recommended, some studies ndicate that an IV infusion of phenytoin may be feasible if proper precautions are observed, such as a suitable vehicle (eg, 0.9% sodium chloride or Ringer's lactated injection), appropriate concentration, preparing the infusion shortly before administration, and using an inline filter; according to most studies, a 0.22 micron inline filter is required[1,3]; phenytoin sodium (250 mg/5mL in a 5 mL syringe) was filtered at a rate of 1 mL/min through a 5 micron stainless steel depth filter without significant reduction in potency.[2] |
| Ranibizumab (*Lucentis*) | Vascular endothelial growth factor antagonist | 5 micron | Withdraw the solution from the vial through a 5-micron, 19-gauge filter needle attached to a 1 mL tuberculin syringe; for intravitreal injection only. |
| Respiratory syncytial virus immune globulin, IV (RSV-IVIG) (*RespiGam*) | Immune globulin | Larger than 15 micron | An inline filter may be used for RSV-IGIV infusions. |
| Streptokinase (*Streptase*) | Thrombolytic enzyme | 0.8 micron or larger | |
| Thiotepa (*Thioplex*) | Antineoplastic agent | 0.22 micron | Filter prior to administration; polysulfone membrane (*Gelman's Sterile Acrodisc*, Single Use) or triton-free mixed ester of cellulose/PVC (*Millipore's MILLEX*-GS Filter Unit) are recommended by the manufacturer. |
| Tositumomab and iodine $^{131}$ I-tositumomab (*Bexxar*) | Radioimmunotherapeutic monoclonal antibody | 0.22 micron | Administer via IV tubing set with an inline filter. The same IV tubing set and filter must be used throughout the entire dosimetric or therapeutic step; a change in filter can result in loss of drug. |
| Vaccinia immune globulin IV (*VIGIV*) | Immune globulin | 0.22 micron | Administer VIGIV via an IV catheter with an administration set that contains an inline filter. |
| Verteporfin (*Visudyne*) | Ophthalmic phototherapy agent | 1.2 micron | Administer using a syringe pump and inline filter; use of an inline filter (pore size 0.22 to 1.2 microns) is required for administration.[1] |

[a]Note: For consistency, the term "micron" is used to encompass all terms meaning the same (eg, micrometer, mcm, mm)

### References

1. Gahart BL, Nazareno AR. *Intravenous Medications: A Handbook for Nurses and Health Professionals.* 23rd ed. St. Louis, MO: Mosby Elsevier; 2006.

2. Trissel LA. *Handbook on Injectable Drugs.* 4th ed. Bethesda, Maryland: American Society of Health-System Pharmacists; 2007.

3. *Drug Facts and Comparisons.* Drug Facts and Comparisons 4.0 [online]. 2007. Available from Wolters Kluwer Health, Inc. Accessed March 9, 2007.

# The use of integral fluid filters in single-use infusion administration sets

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November 2008

*NOTE: the research in this paper has not been updated since 2008.*

## Introduction

This report has been produced to investigate recommendations for the use of in-line filters in IV administration sets. It sets out to clarify whether filters are required at all and if so, what pore size is recommended.

In-line fluid filters may be used within an IV administration set in an attempt to prevent (or delay) phlebitis. Phlebitis is inflammation of the vein which can be painful and can result in fever. It can be caused in the following ways:

- Infectious agents enter the patient's vein via the administration of fluids/medication which can be the cause of nosocomical infection
- Undiluted or undissolved drug can enter the patient and damage the vein (chemical irritation)
- Particles of plastic or steel (from administration equipment such as tubing or needles) can cause vascular damage (mechanical irritation) (Falchuk et al. 1985)

All commercially available pharmaceutical IV fluids are filtered to at least 0.45 microns at the end of the manufacturing process (communication with member of UK Parenteral society). Fluids with heat-labile components are sterilised by filtration and all other fluids are terminally sterilised. If a solution requires bacterial filtration during administration, the filter must have a pore size no larger than 0.2 microns (RCN guidelines, 2005). NICE guidelines recommend that in-line filters should not be used routinely for infection control purposes during infusion through central venous catheters (NICE guidelines, 2003) although no similar recommendations could be found relating specifically to peripheral intravenous catheters. The issue of bacterial retention filters impeding the flow of some solutions has also been raised (Dunleavy and Sevick, 2001).

## Filtration properties of IV filters

Research has shown that patients undergoing IV infusions are at far greater risk of developing infusion-related phlebitis than infusion-related infection (Roberts et al. 1994). One laboratory study indicated that a patient is likely to be infused with more than 107 particles during a 24 hour session of IV therapy (Backhouse et al. 1987). Studies using IV filters reveal that much of the particulate matter that enters the patient's vein goes unnoticed because of its size and appearance (Stromberg and Wahlgren, 1989). These particles include scrapings of plastic that may peel off the walls of the plastic tube and enter fluid upon injection of medication as well as precipitations within the fluid. These filters may also remove chemical particulates that have remained undissolved in the fluid. Filters which are used to remove particulate matter of this nature have much larger pore sizes than bacterial filters. Pore sizes for particulate filters range from approximately 15 microns (British standard 8536) to 45 microns (Chamberland et al. 1976)

Published studies investigating the benefits of in-line filters on the incidence of phlebitis in patients have focused mainly on bacterial filters. One randomised study used a bacterial in-line filter (0.22 microns) and reported that patients had a 75% chance of being phlebitis-free after 3 days (sets were changed each day) whereas they had only a 42% chance if the filter was not used (Falchuk et al. 1985). Another randomised study (Allcutt et al. 1983) found that the use of a 0.22 micron filter delayed the onset of phlebitis in patients and this was particularly marked in patients who were being administered antibiotics. Other investigators reported significantly less cases of phlebitis when an in-line filter was used compared to infusions with no filter (Chee and Tan, 2002). Another study (Roberts et al. 1994) found that an in-line microbial filter (0.22 microns) was as effective as heparin/hydrocortisone administration in reducing the occurrence of phlebitis when administering IV antibiotics to patients with cystic fibrosis. However, not all studies found a difference in phlebitis rates between filter groups and controls (Maddox, 1983).

Most of the research in this area has been carried out on bacterial filters and there is very little data reviewing the benefits of filters with larger pore-sizes. One investigation found no decrease in phlebitis rates when using a filter of a larger pore size of 45 microns (Chamberland et al. 1976). Another found no significant difference in phlebitis rates between a 5 micron filter group and 'no-filter' control group whereas a difference was seen between the control group and a '0.45 micron filter' group indicating that filters with smaller pore sizes appear to be more effective in reducing phlebitis rates. (Rusho, 1979). Research indicates that IV fluids contain significantly more smaller particles (less than 2 microns) than larger particles (larger than 40 microns) but what is not clear from the literature is whether larger particles cause more damage.

The Cochrane Collaboration (Foster et al. 2006) carried out a literature review of studies investigating whether in-line filters prevented death or morbidity in neonates with IV lines. They concluded that there was insufficient evidence to link the use of in-line filters with improved clinical outcomes in this patient group.

## Standards

There are a range of standards currently used in the UK which relate to the requirement of fluid filters within administration sets for the filtration of larger particles. The section below summarises the relevant standards.

### Standard: BS 2463: Part 2:1989

Title: Transfusion equipment for medical use: Part 2: Specification for administration sets
Scope: Administration sets (for blood and other fluids). All administration sets shall include a 'filter enclosed in a transparent chamber'. The filter chamber may be integral with the drip chamber.
Filter specifications: Administration sets for use with IV fluid other than blood should have a pore diameter that prevents the passage of particles of a size of 40 microns or greater.

### Standard: BS EN ISO 8536-4:2007

Title: Infusion equipment for medical use. Part 4: Infusion filters for use, gravity feed
Scope: Gravity feed infusion sets. Components of solution sets include a fluid filter.
Filter specification: 'Generally fluid filter used has nominal pore size of 15 microns'

### Standard: BS EN ISO 8536-8:2004

Title: Infusion equipment for medical use. Part 8: Infusion equipment for use with pressure infusion apparatus. (For use with IV pumps, pressures of up to 200 kPa)
Scope: General requirements of vented and non-vented infusion sets. Components of infusion sets include a fluid filter.
Filter specification: 'Generally fluid filter used has nominal pore size of 15 microns'

## Standard: BS EN ISO 8536-11:2004

Title: Infusion equipment for medical use. Part 11: Infusion filters for use with pressure infusion equipment
Scope: The fluid filters within pressure infusion sets
Filter specification: Includes design and performance specifications (for example, filter housing should be transparent and possess a venting system in case of blockage by air bubbles). Filter specification does not include effectiveness or separation of particles (no pore size included).

## Confusion between current standards

For many years, the British Standard (BS 2463 part 2) was the relevant UK standard related to administration sets and is still commonly referred to. However, it was withdrawn in 2007 and the European ISO standard (BS EN ISO 8536) was adopted in the UK. The BS 2463 specified a filter with a pore size of 40 microns or less whereas the BS EN ISO 8536 states that, in general, filters have a 'nominal' pore size of 15 microns.

A summary of the relevant standards are shown in the table below:

| Standard | Status | Title | Filter specification |
|---|---|---|---|
| BS 2463: Part 2:1989 | Withdrawn March 2007 | Specification for administration sets Pore size of 40 microns or less | Pore size of 40 microns or less |
| BS EN ISO 8536-4:2007 | Current | *Infusion filters for use, gravity feed* | *Generally the filter used has a* nominal pore size of 15 microns |
| BS EN ISO 8536-8:2004 | Current | Infusion equipment for use with pressure infusion apparatus | Generally the filter has a nominal pore size of 15 microns |
| BS EN ISO 8536-11:2004 | Current | Infusion equipment for use with pressure infusion equipment. Part 11: Infusion filters for use with pressure infusion equipment | Filter specification does not include effectiveness or separation of particles (no pore size included). |

## Recommendations

The RCN make the following recommendations:

> *Use of filters should adhere to the manufacturer's guidelines and the filtration requirements of the therapy*
> *For non-lipid-containing solutions that require filtration, an additional 0.2 micron filter containing a membrane that is both bacteria/particulate-retentive and air-eliminating should be used. All infusion sets should contain in-line filtration appropriate to the solution being administered. Clear fluids require 15 micron filtration (or less) which is usually provided by a standard clear fluid set. .*
> *For lipid infusions or total nutrient preparations that require filtration, a 1.2 micron filter containing a membrane that is both bacteria/particulate-retentive and air-eliminating should be used.* (Section 4.3, RCN 2005)

*The administration set used to administer IVIG (Intravenous immunoglobulins) should have a 15 micron filter to prevent infusion of undissolved immunoglobulin or other foreign material into the patient.* (Section 8.9, RCN 2005)

The RCN provide the additional guidelines for the administration of parenteral nutrition :

> *Parenteral nutrition solutions not containing lipids should be filtered with a 0.2 micron filter during administration, or as specified in the product information .*
> *Parenteral nutrition solutions containing lipid emulsion should be filtered using a 1.2 micron filter during administration, or as specified in the product information.*(Section 8,5 RCN, 2005)

The Centre for Disease Control and Prevention (CDC) made the following statement in a MMWR report (O'Grady et al. 2002):

> *'Infusate-related BSI is rare'*

and they highlight the fact that some solutions can block the filter. The authors recommend filtration by pharmacy as a 'practical and less costly way to remove the majority of particulates' .

The Infection Control nurses association (ICNA) published 'Guidelines for preventing intravascular catheter-related infection' in 2001. They did not issue specific guidelines about filter use however, stating that they are 'commonly used to administer IV drugs of high molecular size to reduce the risk of phlebitis and accidental air administration into the circulatory system. However their use in preventing CR-BSI remains controversial' (ICNA, 2001).

# Conclusion

It is clear from the literature reviewed here that filters can play a useful role in preventing and reducing phlebitis. However, up to date clinical data on large-pore filters is sparse and further research in this area would clearly be beneficial.

Whenever infusion sets are used to administer solutions, instructions for use should be followed for both the device and the medicinal product. If compliance with an appropriate standard is claimed on the packaging, then any requirement for a filter should be adhered to by the manufacturer. However, as standards are voluntary, many manufacturers do not claim or test for compliance with relevant standards

The MHRA have advised SMTL (personal communication) that the decision ultimately lies with the healthcare professional, based on best practice as to whether an in-line filter is required and what pore size is appropriate for that particular therapy.

In conclusion, although there is some good clinical evidence for the role of bacterial retention filters in reducing phlebitis, and guidelines exist for clinicians in determining which filters are appropriate for certain fluids, we have been unable to find guidelines which clearly state the circumstances in which filters should be used.