


Subcutaneous Drug Infusion Compatibility Guidelines

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Gippsland Region Palliative Care Consortium Clinical Practice Group



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| <i>Policy No.</i> | GRPCC-CPG003_1.1_2016 |
| <i>Title</i> | Subcutaneous Drug Infusion Compatibility Guidelines |
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| <i>Purpose</i> | This guideline has been endorsed by the GRPCC Clinical Practice Group and is based on current evidence and best practice components. It is recommended this guideline be used to inform health services policies and procedures regarding injectable medication and continuous subcutaneous infusions in clinical practice across the region. |

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Policy Statement

In palliative care clinical practice, the oral route of administration is the preferred option. However, when the parenteral route is required, the subcutaneous route should be the first option. Drugs may be given as infusions over 24 hours or as bolus doses.

The combination of drugs for subcutaneous infusions must be checked for compatibility prior to prescription and administration of injectable medication.

This guideline must be used in conjunction with its companion document **The Eastern Metropolitan Region Palliative Care Consortium (Victoria) Syringe Driver Drug Compatibilities-Practice Guidelines 2016¹**, or when more information is required regarding other drug compatibility data and combinations. This companion document contains more extended evidenced based information on many of the elements related to safe use of drug combinations in continuous subcutaneous infusions/syringe drivers.

If the combination is not listed in this guideline or its companion document consult:

1. Dickman A., Schneider J., Varga J. The syringe driver continuous subcutaneous infusions in palliative care 3rd Ed. , Oxford University Press, 2011 (1)
2. The syringe driver database www.palliativedrugs.com

Definitions

Drugs which CAN be administered subcutaneously:

| | | |
|----------------|---|-----------------|
| cyclizine | clonazepam | dexamethasone |
| fentanyl | hyoscine butylbromide & hyoscine hydrobromide | |
| glycopyrrolate | haloperidol | hydromorphone |
| ketamine | ketorolac | levomepromazine |
| metoclopramide | methadone | midazolam |
| morphine | octreotide | ondansetron |
| oxycodone | phenobarbitone | |

The drug compatibilities documented in this guideline are collated from published literature. The criteria for the selection of compatibilities into this guideline included at least two of the following;

- published in a journal or hospital newsletter;
- published in a reference book;
- laboratory analysis;
- documented concentrations; and
- documented use in a clinical setting.

¹ <http://www.emrpcc.org.au/wp-content/uploads/2016/05/Syringe-Driver-Drug-Compatibilities-2016-May-3-final.pdf>

Procedure

1. Subcutaneous infusions will be initiated in accordance with each organisation subcutaneous administration of medication policy
2. Check the compatibility table and references of the different drugs before commencing
3. Infusion site:
 - a. A plastic teflon or vialon cannula should be used rather a metal butterfly needle to minimise the risk of site inflammation (*saf-T-intima is a commonly used device*²).
 - b. Infusion sites may last up to seven days, depending on the drugs/combination used;
 - c. Routine rotation site every 72 hours reduces the risk of site problems; and
 - d. The site should be changed more regularly e.g. 24-48h if it becomes painful and/or inflamed
4. Number of drugs in infusion

No more than two drugs should be combined in an infusion **except** for the following combinations:

 - a. Morphine, Metoclopramide and Haloperidol;
 - b. Morphine, Metoclopramide, Midazolam; and
 - c. Morphine/Hydromorphone, Haloperidol, Midazolam, and Metoclopramide.

The administration of other drug combinations may be considered if there is supporting literature for drug compatibility.

5. Diluent for infusions
 - a. Sodium Chloride 0.9% is the preferred diluent as it produces a solution which is as close to physiological tonicity as possible
 - b. The main exceptions to this rule are solutions containing cyclizine, in which case Water for Injection should be used.
6. Storage conditions for drug infusions

Infusions (syringe drug/s combinations) should be prepared immediately prior to commencement of infusion.

Syringes containing any drug or drugs combinations should be protected from light e.g. by placing the syringe driver in a pouch.
7. Duration of Infusion

The duration of drug infusions should be limited to 24 hours. However, if circumstances require otherwise (e.g. in the community) the duration of the infusions may be extended pending on stability data in published literature and client's symptom stability.
8. Drugs NOT suitable for subcutaneous administration
 - a. Phenothiazine's - prochlorperazine (Stemetil), chlorpromazine (Largactil) promethazine (Phenergan) - too irritant

- b. Phenytoin
 - c. Diazepam - absorbed onto PVC. Precipitates at certain dilutions
9. Potential problems to consider
- a. Phenobarbitone sodium - can be too irritant if not well diluted - pH 8.5 – 10
 - b. Clonazepam - significant loss of clonazepam occurs when infused through PVC tubing, hence it tends not to be given as a continuous subcutaneous infusion
 - c. Cyclizine, levomepromazine and ketamine tend to be infused alone, rather than in combination with other drugs due to cost considerations.

² <https://www.bd.com/europe/safety/en/pdfs/Saf-T-Intima%20use%20Guide.pdf>

References

1. Dickman A, Schneider J, Varga J. The syringe driver: continuous subcutaneous infusion in palliative care. 3rd Ed. Oxford: Oxford University Press; 2011 (9)
2. Syringe Driver Drug Compatibilities- Practice Guidelines 2016 Eastern Metropolitan Region Palliative Care Consortium (Victoria)*Clinical Working Party*
3. Syringe Driver Compatibility Table. The Palliative Care Handbook: *Guidelines for clinical management and symptom control* 2014 pages 150-151
4. Palliative Care Therapeutic Guidelines. Version 3, 2010
5. Syringe Driver - Drug Compatibility database. Palliative Care Matters <http://www.pallcare.info>
6. Gardiner PR. Compatibility of an injectable oxycodone formulation with typical diluents, syringes, tubings, infusion bags and drugs for potential co-administration. *Hospital Pharmacist* Sept 2003;10:354-361
7. Palliative Drugs www.palliativedrugs.com
8. Twycross R., & Wilcock A. Palliative Care Formulary 5th Edition Nottingham. Palliativedrugs.com Ltd; 2014
9. Trissel's 2 Clinical Pharmaceutic Database (Parenteral Compatibility). (2007) Micromedex [On-Line] <http://micromedex.hcn.net.au>
10. GRPCC-CPG002_1.0_2014 - Opioid Conversion Guidelines. Available online from www.grpcc.com.au

Key Performance Indicator

100% of drugs in a subcutaneous infusion are checked for compatibility before the preparation and administration of the prescribed combination.

Considerable information contained in this guideline was taken from CALVARY HEALTH CARE BETHLEHEM related document, when this guideline was first developed.

Drug Compatibility in Subcutaneous Infusions Chart in Standard Forms

| | Cyclizine | Dexamethasone | Fentanyl | Glycopyrrolate | Haloperidol | Hydromorphone | Hyoscine Butylbromide | Hyoscine Hydrobromide | Ketamine | Ketorolac | Levomepromazine | Metoclopramide | Methadone | Midazolam | Morphine Sulphate | Octreotide | Ondansetron | Oxycodone | Phenobarbitone Sodium |
|-----------------------|-----------|---------------|----------|----------------|-------------|---------------|-----------------------|-----------------------|------------|-----------|-----------------|----------------|-----------|------------|-------------------|------------|-------------|------------|-----------------------|
| Cyclizine | pH 3-3.7 | ⚠ | ? | ✔ | ✔ | ✔ | ⚠ | ✔ | ? | ? | ✔ | ? | ? | | ⚠ | ✔ | ✔ | ✔ | ? |
| Dexamethasone | ⚠ | pH 7-8.5 | ? | ? | ⚠ | ⚠ | ✔ | ✔ | ✔ | | ⊘ | | ✔ | ⊘ | ⚠ | | ⚠ | ✔ | ⊘ |
| Fentanyl | ⚠ | ? | pH 4-7.5 | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | | ? | ✔ | ? | ✔ | ? | ✔ | ✔ | ? | ✔ |
| Glycopyrrolate | ✔ | ? | ✔ | pH 2.3-4.3 | ✔ | ✔ | ✔ | NA | ✔ | | ✔ | ✔ | ✔ | ✔ | ✔ | ? | ✔ | ✔ | ⊘ |
| Haloperidol | ✔ | ⊘ | ✔ | ✔ | pH 2.8-3.6 | ⚠ | ✔ | ✔ | ✔ | ⊘ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ? |
| Hydromorphone | ⚠ | ⚠ | ✔ | ✔ | ⚠ | pH 4-5.5 | ✔ | ✔ | ✔ | ⚠ | ✔ | ✔ | ? | ✔ | NA | ✔ | ✔ | NA | ? |
| Hyoscine Butylbromide | ⚠ | ? | ✔ | ? | ? | ? | pH 3-5.5 | ? | ✔ | ? | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ? |
| Hyoscine Hydrobromide | ✔ | ✔ | ✔ | NA | ? | ✔ | ? | pH 4 | ✔ | | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ? |
| Ketamine | ? | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | pH 3.5-5.5 | | ✔ | ✔ | ✔ | ✔ | ✔ | ? | ? | ✔ | ? |
| Ketorolac | | | | | ⊘ | ⚠ | | | | pH 7-8 | | | ✔ | ? | ✔ | ? | ? | | ? |
| Levomepromazine | ✔ | ⚠ | ? | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ? | pH 3-5 | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ? |
| Metoclopramide | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | | ? | pH 3-6.5 | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ? |
| Methadone | ? | ✔ | ? | ✔ | ✔ | ? | ? | ✔ | ? | | ✔ | ✔ | pH 4.5-7 | ✔ | ? | ? | ? | ✔ | ⊘ |
| Midazolam | ? | ⊘ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | | ✔ | ✔ | ✔ | pH 2.9-3.7 | ⚠ | ✔ | ✔ | ✔ | ? |
| Morphine Sulphate | ✔ | ✔ | ? | ✔ | ✔ | NA | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ? | ✔ | pH 2.5-6 | ✔ | ✔ | NA | ? |
| Octreotide | ⚠ | ⚠ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ⚠ | ⚠ | ✔ | ? | ✔ | ✔ | pH 3.5 | ✔ | ✔ | ? |
| Ondansetron | ⚠ | ⚠ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | | ✔ | ✔ | ? | ✔ | ✔ | ✔ | pH 3.9-4.5 | ✔ | ? |
| Oxycodone | ⚠ | ✔ | ? | ✔ | ✔ | NA | ✔ | ✔ | ✔ | ? | ✔ | ✔ | ? | ✔ | NA | | ✔ | pH 4.5-5.5 | ? |
| Phenobarbitone Sodium | ? | ? | ? | ⊘ | ? | ? | ? | ? | ? | ? | ? | ? | ⊘ | ? | ? | ? | ? | ? | pH 8.5-10.5 |

KEY Incompatible Compatible Sometimes incompatible (usually at higher concentrations) - observe carefully Unknown **NA** not usually used together

- Please note:**
- This table should be used as a general guide only as high concentrations of drug combinations will affect the compatibility of the desired infusion. Vigilance is required in all cases.
 - pH may vary with different formulations; check product information or consult the manufacturer.
 - Where there is no symbol indicating medication compatibility OR unknown symbol, it is not recommended for use, or proceed with caution and closely monitor administration site.

References:

- Dickman A, Schneider J, Varga J. The syringe driver: continuous subcutaneous infusion in palliative care 3rd Ed. Oxford: Oxford University Press; 2011
- Palliative Care Therapeutic Guidelines. Version 3, 2010 Syringe Driver Compatibility Table.
- The Palliative Care Handbook: Guidelines for clinical management and symptom control 2014 pages 150-151
- Syringe Driver - Drug Compatibility database. Palliative Care Matters. <http://www.pallcare.info>
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- Trissel's 2 Clinical Pharmaceutical Database (Parenteral Compatibility). [2007] Micromedex [On-Line] <http://micromedex.hcn.net.au>