WHO Access and Control Newsletter

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The Access and Control Newsletter is sent by the World Health Organization, Department of Essential Medicines and Health Products,
Medicine Access and Rational Use Unit.
The Newsletter provides you with the latest news from WHO on access to medicines controlled under the international drug treaties, both with regards to evaluation of substances for their dependence producing properties, and to improving access for medical use to medicines made from these substances

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Alert on paediatric morphine dosages

An alert was published in the WHO Pharmaceuticals Newsletter, No 4, 2012, pages 23 -26 on morphine dosages for children. New dosage recommendations are now available in the WHO Guidelines on the Pharmacological Treatment of Pain in Children with Medical Illness. The new guidelines have a more cautious approach and replace the dosage recommendations in the WHO Model Formulary for Children (2010). In view of these new Guidelines, the dosage recommendations for morphine and other opioid analgesics in children in future editions of other relevant publications (text books, hand books etc.) may need to be reconsidered as well. WHO has no recently published guidelines on the use of opioid analgesics in adults, but several aspects may also apply to their prescription to adults. Please see the annex for full details.

For details see the article in the WHO Pharmaceuticals Newsletter. The alert will also be published in the next issue of the WHO Drug Monitor.

For the convenience of the reader it is also attached to this Newsletter as an annex.

Scoping document for WHO Guidelines for persisting pain in adults

In August 2012, WHO defined what will be in the guidelines for the pharmacological treatment of persisting pain in adults with medical illnesses. A scoping document with this purpose was approved by the WHO Guidelines Review Committee, the overseeing body for the quality assurance of WHO treatment guidelines. The document is entitled Scoping document for the WHO guidelines for the pharmacological treatment of persisting pain in adults with medical illnesses.

In spite of its confinement to pharmacological treatment, the guidelines will be broad and address a wide range of conditions that have pain as a symptom. The scoping document defines working methods, clinical questions and health systems questions to find the answer and its evidence, budget and timelines.

Subject to the availability of funding, it is foreseen that these guidelines will be ready by Spring 2015.

A Spanish version of the WHO policy guidelines

A Spanish version of the WHO policy guidelines *Ensuring Balance in National Policies on Controlled Substances, Guidance for Availability and Accessibility of Controlled Medicines* has now been published. It is entitled *Garantizando el equilibrio en las políticas nacionales sobre sustancias fiscalizadas, Orientación para la disponibilidad y accesibilidad de los medicamentos fiscalizados*. It provides 21 guidelines on policies and legislation with regards to availability, accessibility, affordability and regulation of controlled medicines.

An electronic version in Spanish, as well as the other 14 languages published previously, may be downloaded free of charge at www.who.int/medicines/areas/quality_safety/guide_nocp_sanend/en/index.html Please note that the reference list is a separate document. Hardcopies of the WHO Policy Guidelines in Spanish can be pre-ordered at the WHO Bookshop and will be shipped in November.

This translation was made possible by the Open Society Foundations and the International Association for Hospice and Palliative Care.

See also our controlled medicines website

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For further information:
Willem Scholten, PharmD MPA
Team Leader, Access to Controlled Medicines
Department of Essential Medicines and Pharmaceutical Policies
World Health Organization, Geneva, Switzerland
Phone: +41 22 79 15540,
e-mail : scholtenw@who.int

Annex

Paediatric morphine dosages

New dosage recommendations are now available in the WHO Guidelines on the Pharmacological Treatment of Pain in Children with Medical Illnesses, published earlier in 2012.[1] The new Guidelines have a more cautious approach and replace the dosage recommendations in the WHO Model Formulary for Children (2010)[2]. In view of these new Guidelines the dosage recommendations for morphine and

[1] World Health Organization, WHO Guidelines for the Pharmacological Treatment of Persisting Pain in Children with Medical Illness World Health Organization, Geneva 2012, ISBN 978 92 4 154812 0. http://www.who.int/medicines/areas/quality_safety/guide_on_pain/en/index.html and http://whqlibdoc.who.int/publications/2012/9789241548120_Guidelines.pdf (permanent URL)

[2] World Health Organization, WHO Model Formulary for Children, Geneva 2010, p 23 and 291.

other opioid analgesics in children in future editions of other relevant publications (text books, hand books etc.) may need to be reconsidered. WHO has no recently published guidelines on the use of opioid analgesics in adults, but the following may also apply to their prescription to adults:

Pain treatment with strong opioids should be based on a low initial dosing. (See tables 1 to 3 for pediatric starting dosages.) Titration of the dosage should be based on a regular assessment of the pain level. This assessment is discussed in the Guidelines. After a starting dose according to the Guidelines, the dosage should be adjusted to the level that is effective (with no ceiling or maximum dose), but the maximum dosage increase is 50% per 24 hours in outpatient settings. Experienced prescribers can increase up to 100% with close monitoring of the patient, increasing to the level that is effective.

The preferred route is oral. If oral administration is not possible, subcutaneous administration or other parenteral routes can be considered, but intramuscular administration should be avoided as it is painful. It should be noted that, due to the first pass effect, parenteral administration is about twice as potent as oral administration.

The dose titration schedule mentioned above also applies to most other strong opioids as well, but not to methadone because of its long half-life. Details for titrating methods for methadone that avoid accumulation can be found in the Guidelines.

In case of overdosage of opioids, the antagonist naloxone can be administered.

Occurrence of dependence is often not well understood. On adequate treatment of pain, it is rare, if occurring at all. However, if opioids are withdrawn abruptly in chronic treatment, severe withdrawal symptoms will be precipitated. Therefore, when stopping treatment, the patient should be weaned gradually: after short-term therapy (7–14 days), the dose can be decreased by 10–20% of the original dose every 8 hours, increasing gradually the time interval between doses. After long-term therapy, the dose should be reduced not more than 10–20% per week.

Pharmacological profiles for morphine and several other opioid and non-opioid analgesics, as well as for the antagonist naloxone can be found in Annex 1 of the Guidelines (page 63). The Guidelines can be downloaded from the web free of charge. The printed Guidelines package contains also a pocket dosing card and pain assessment scales for children.

Table 1. Starting dosages for opioid analgesics for opioid-naive neonates

Medicine	Route of administration	Starting dose
Morphine	IV injection[a]	25–50 mcg/kg every 6 hrs
	SC injection	
	IV infusion	Initial IV dose[a] 25–50 mcg/kg, then 5–10 mcg/kg/hr
Fentanyl	IV injection[b]	1–2 mcg/kg every 2–4 hrs[c]
	IV infusion[b]	Initial IV dose[c] 1–2 mcg/kg, then 0.5–1 mcg/kg/hr

[a] Administer IV morphine slowly over at least 5 minutes.

[b] The intravenous doses for neonates are based on acute pain management and sedation dosing information. Lower doses are required for non-ventilated neonates.

[c] Administer IV fentanyl slowly over 3─ 5 minutes.

Table 2. Starting dosages for opioid analgesics in opioid-naive infants (1 month–1 year)

Medicine	Route of administration	Starting dose
Morphine	Oral (immediate release)	80–200 mcg/kg every 4 hrs
	IV injection [a]	*1–6 months:* 100 mcg/kg every 6 hrs *6–12 months:* 100 mcg/kg every 4 hrs (max 2.5 mg /dose)
	SC injection	
	IV infusion [a]	*1–6 months:* Initial IV dose: 50 mcg/kg, then: 10–30 mcg/kg/hr *6–12 months:* Initial IV dose: 100 - 200 mcg/kg, then: 20–30 mcg/kg/hr
	SC infusion	1–3 months: 10 mcg/kg/hr 3–12 months: 20 mcg/kg/hr
Fentanyl [b]	IV injection	1–2 mcg/kg every 2–4 hrs[c]
	IV infusion	Initial IV dose 1–2 mcg/kg[c], then 0.5–1 mcg/kg/hr
Oxycodone	Oral (immediate release)	50–125 mcg/kg every 4 hours

[a] Administer IV morphine slowly over at least 5 minutes.

[b] The intravenous doses of fentanyl for infants are based on acute pain management and sedation dosing information.

[c] Administer IV fentanyl slowly over 3–5 minutes.

Table 3. Starting dosages for opioid analgesics in opioid-naive children (1–12 years)

Medicine	Route of administration	Starting dose
Morphine	Oral (immediate release)	1–2 years: 200–400 mcg/kg every 4 hrs 2–12 years: 200–500 mcg/kg every 4 hrs (max 5 mg)
	Oral (prolonged release)	200–800 mcg/kg every 12 hrs
	IV injection [a]	1–2 years: 100 mcg/kg every 4 hrs 2–12 years: 100–200 mcg/kg every 4 hrs (max 2.5 mg)
	SC injection	
	IV Infusion	Initial IV dose : 100-200mcg/kg [a], then 20–30 mcg/kg/hr
	SC Infusion	20 mcg/kg/hr
Fentanyl	IV injection	1–2 mcg/kg [b], repeated every 30–60 minutes
	IV Infusion	Initial IV dose 1–2 mcg/kg [b], then 1 mcg/kg/hr
Hydromorphone [c]	Oral (immediate release)	30–80 mcg/kg every 3–4 hrs (max 2 mg/dose)
	IV injection [d] or SC injection	15 mcg/kg every 3–6 hrs
Methadone [e]	Oral (immediate release)	100–200 mcg/kg every 4 hrs for the first 2–3 doses, then every 6–12 hrs (max 5 mg/dose initially) [f]
	IV injection[g] and SC injection	
Oxycodone	Oral (immediate release)	125–200 mcg/kg every 4 hours; max 5 mg/dose)
	Oral (prolonged release)	5 mg every 12 hours

[a] Administer IV morphine slowly over at least 5 minutes.

[b] Administer IV fentanyl slowly over 3─5 minutes.

[c] **Hydromorphone is a potent opioid and significant differences exist between oral and intravenous dosing. Use extreme caution when converting from one route to another.** In converting from parenteral hydromorphone to oral hydromorphone, doses may need to be titrated up to 5 times the IV dose.

[d] Administer IV hydromorphone slowly over 2─3 minutes.

[e] Due to the complex nature and wide inter-individual variation in the pharmacokinetics of methadone, methadone should only be commenced by practitioners experienced with its use.

[f] Methadone should initially be titrated like other strong opioids. The dosage may need to be reduced by 50% 2─3 days after the effective dose has been found to prevent adverse effects due to methadone accumulation. From then on dosage increases should be performed at intervals of one week or over and with a maximum increase of 50%.

[g] Administer IV methadone slowly over 3─5 minutes.