

# Infúzne podávanie svetlocitlivých liečiv

## XXVIII. Kongres nemocničného lekárstva

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# Čo nás čaká

Vlastnosti  
určujúce  
svetlocitlivosť

Čo sa môže  
stať

Ako chrániť

Liečivá

## Vlnová dĺžka

- Spektrum viditeľného a UV žiarenia: 200-800 nm
- Žiarenie s vysokou energiou: 290-400nm
- Rôzne látky – absorpcia v rôznych častiach spektra
- Jantárové sklo – neprepúšťa pod 400 nm

# pH

- Fotostabilita ovplyvnená aj excipientami
- V závislosti od ionizácie - určenie pH a pufru
- Veľmi často fosfátový pufor
- Pri nedodržaní pH – rýchlejší rozklad

# Zriedenie

Koncentrované  
roztoky: efekt  
vnútorného filtra

Zriedené roztoky:  
veľký povrch,  
nízka koncentrácia

# Čo sa môže stať

- Zmena farby
- Zmena viskozity
- Precipitácia
  
- Zníženie/strata účinku lieku
- Vedľajšie/nežiaduce účinky

# Ako chrániť pred svetlom

Hlavne  
pri kontinuálnych  
infúziách

Chrániť vak,  
infúzne sety

Zabalenie  
striekačky  
do alumíniového  
obalu

# Administrácia: chrániť – nechrániť?

Cefotaxím – infúzia 20-60 min

Adrenalin – okamžité podanie

Hydrokortizón

Digoxín

Linezolid – chránené až do času podania

Fotemustín

Cisplatina

Dakarbazín

Danorubicín





REVIEW

## Review of the Stability of Photosensitive Medications<sup>☆</sup>

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### KEYWORDS

Stability;  
Photosensitive  
medications;  
Review

### Abstract

**Objectives:** Identify the photosensitive drugs included in the hospital pharmacotherapeutic guide and search for stability data on the storage, reconstitution, and dilution of these compounds.

**Methods:** The data were obtained by referencing technical specifications, information provided by drug laboratories, and in some cases, we performed a more extensive bibliographic search (tertiary sources and conference lectures) for each particular medication. We also performed a data search on the PubMed information database (from 2004 to 2009).

The drugs were placed in alphabetical order by brand since the stability of each drug when exposed to light does not depend exclusively on the primary active ingredient. Eight columns describe the principal characteristics of the drugs: brand name, active ingredient, laboratory, storage, reconstitution and dilution conditions, observations, and references.

**Results:** The listing comprised of 139 of the 1954 photosensitive medicines included in the pharmacotherapeutic guide (Table 1).

**Conclusions:** The lack of studies published on the stability of photosensitive medications provided the need for an internal review at our hospital.

It is important for drug-producing laboratories to perform photosensitivity tests on their products, with the results presented in the technical specifications in order to provide more accessible and reliable information. We believe that this should be required by law.

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### PALABRAS CLAVE

Estabilidad:

Revisión de la estabilidad de los medicamentos fotosensibles

Table 1 Review of Photosensitive Drugs.

Brand Name	Active Ingredient	Laboratory	Storage	Reconstitution	Dilution	Observ.	Ref.
ÁC. ASCÓRBICO® (amp)	Vitamin C	Bayer	PFL (it loses 50–60% of its activity in 24 h)	Not applicable	No need to PFL <sup>a</sup> (administer immediately)	Slight colouration does not imply activity alteration	5, 6
ACICLOVIR COMBINO PHARM® (caps/tab)	Acyclovir	Combino Pharm, S.L.	PFL (should be stored in light-resistant packages, 15–25%)	Not applicable	Not applicable	-	7, 8
ACTOCORTINA® (vial)	Hydrocortisone sodium phosphate	Nycomed Pharma	PFL	No need to PFL <sup>a</sup> (administer immediately)	No need to PFL	-	8
ACTRAPID® (vial)	Insulin	Novo Nordisk A/S	PFL	Not applicable	PFL <sup>a</sup> (administer immediately)	-	7
ADRENALINA® (img/ml amp)	Epinephrine	Braun	PFL (cover amp despite it being opaque)	Not applicable	No need to PFL	Dispose of if yellowish in colour (it darkens with oxidation)	8
ADRIAMICINA® (vial)	Doxorubicin or adriamycin	TEDEC MEIJI FARMA	PFL	No need to PFL <sup>a</sup> (stable 24 h)	No need to PFL <sup>a</sup>	Not applicable	7
AGASTRAT® (sol/perf)	Tirofiban	Merck Sharp & Dohme de España, S.A.	PFL	Not applicable	PFL <sup>a</sup> (administer immediately)	-	7
AKINETON® (amp)	Biperiden lactate	DESMA LABORATORIO FARMACÉUTICO, S.L.	PFL	Not applicable	Not applicable	-	9
AMERIDE® (tab)	Amiloride hydrochlorothiazide	Bristol-Myers Squibb	PFL	Not applicable	Not applicable	-	7
ANAFRANIL® (amp)	Clomipramine	Novartis Farmacéutica	PFL	Not applicable	PFL <sup>a</sup> (administer immediately)	-	7
ARANESP® (syr)	Darbepoetin alpha	Amgen Europe B.V.	PFL (stable for 72 h under artificial light – not stable under sunlight)	Not applicable	Not applicable	Do not use if cloudy or has particles	7, 9
AVASTÍN® (vial)	Bevacizumab	Roche Farma S.A	PFL	Not applicable	No need to PFL	-	7
BCNU® (amp)	Carmustine	Bristol-Myers Squibb S.A.	PFL	PFL (stable 7 days)	No need to PFL <sup>a</sup>	-	12, 13, 14, 15
BESILATO DE ATRACURIO® (amp)	Atracurium besylate	Inibsa	PFL	Not applicable	Stable in daylight at concentration of 0.5 mg/ml (no more than 30 °C)	-	8

# Furosemid - podávanie

Perorálne

Bolusová  
injekcia

I.v. infúzia

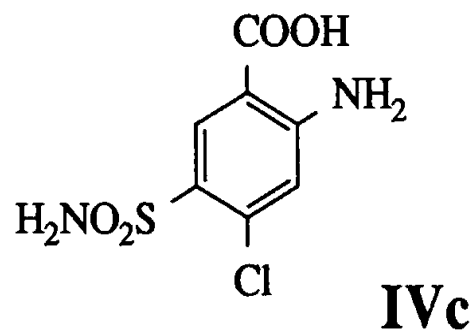
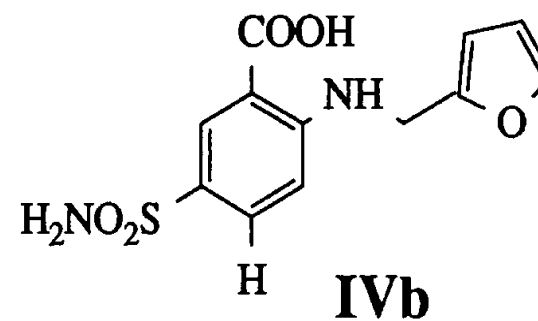
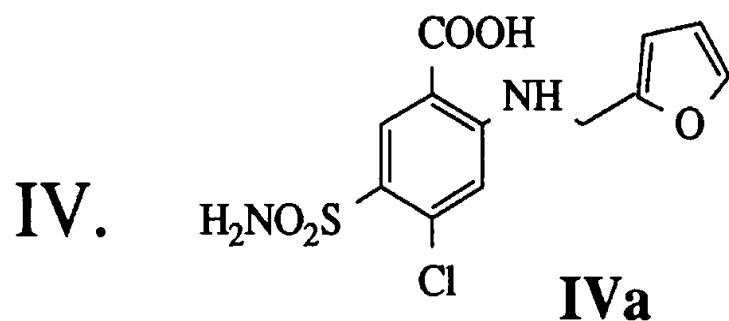
Uchovávať  
chránené  
pred  
svetlom

Furosemid -  
podávanie

I.v. infúzia

Uchovávať  
chránené  
pred svetlom


# Furosemid – dehalogenácia a fotohydrolýza



- Infúzia – max 4mg/min
- 1000mg v 400ml -> podávanie 4 hodiny

Detské kardiocentrum:

- Rýchlosť 10mg v 1ml/hod
- Pri objeme 20 ml -> 20 hodín



Kontinuálna  
infúzia

## SPC

Uchovávať chránené pred svetlom

Sklenené jantárovo žlté ampulky, sklo typu I

Chemická a fyzikálna stabilita - 24 hodín pri 25 °C **pri ochrane pred svetlom**

## Handbook on injectable drugs

Svetlo má degradujúci účinok

Po odstránení obalu sa odporúča injekcie chrániť pred svetlom

## Stabilis

Okrem 7 skúšok, všetky (84) za neprístupu svetla

(caps/susp)								
FENTANEST® (amp)	Fentanyl	Kernpharma	PFL	Not applicable	No need to PFL	-	5	
FLUOROURACILO® (vial)	5-Fluorouracil	Ferrer Farma	PFL	Not applicable	PFL	-	12,13,14, 15	
FOLINATO CÁLCICO GES® (amp)	Calcium folinate	GES	PFL	No need to PFL <sup>a</sup> (administer immediately)	No need to PFL <sup>a</sup> (administer immediately)	-	7	
FUNGIZONA® (vial)	Amphotericin B	Bristol Myers Squibb	PFL	No need to PFL <sup>a</sup> (administer immediately)	No need to PFL	-	7	
FUROSEMIDA INIBSA® (amp)	Furosemide	Inibsa	PFL	Not applicable	PFL	Yellowish colour indicates instability	5, 8	
GENOXAL® (amp)	Cyclophosphamide	Baxter Oncology	PFL	PFL	No need to PFL	-	7	
HALOPERIDOL ESTEVE® (amp)	Haloperidol	Esteve	PFL (stable for 8 h under light)	Not applicable	PFL	-	8	

**Table 4.** Continued

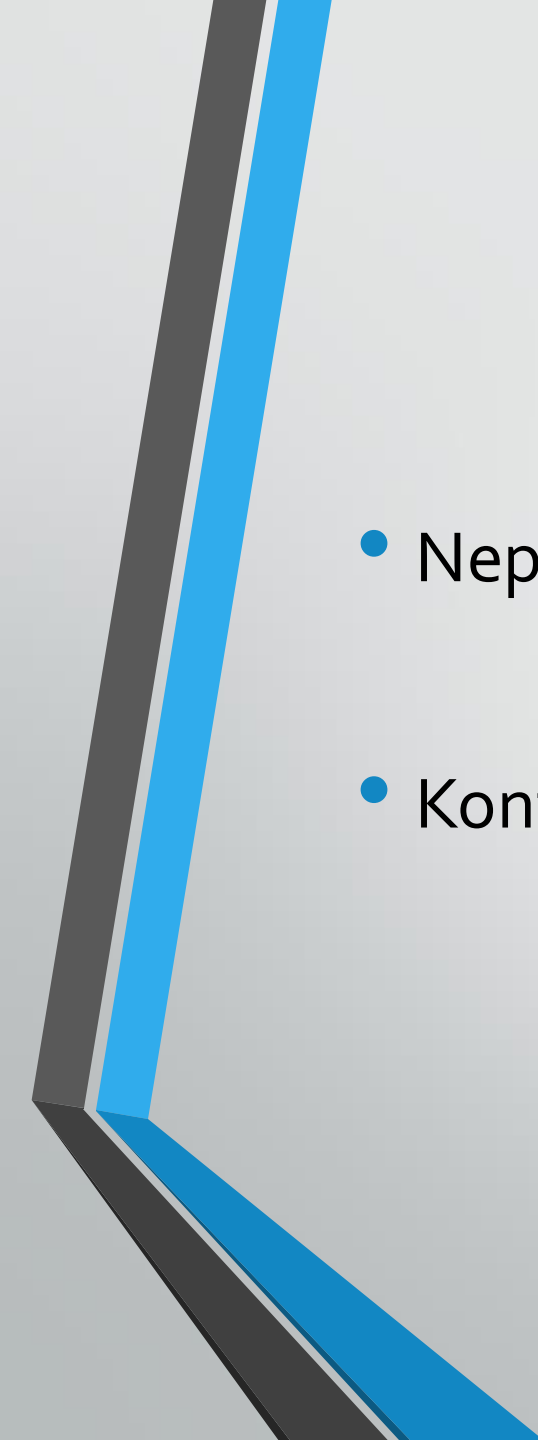
Active Pharmaceutical Ingredient	Formulation	Immediate Container	Light Protection of Formulation	Light Protection of Ready-to-Use Preparation	Source <sup>a</sup>
Epirubicin HCl	Injection	Glass vial	X	X	B
Epoprostenol Na	Powder for infusion	Glass vial	X	X	B
Eptifibatide	Concentrate for infusion	Glass vial	X	NO	B
Estradiol cypionate	Injection	Glass vial	X		A
Etoposide	Concentrate for infusion	Glass vial	X		B
Fentanyl citrate	Injection	Glass ampoule	X		B
Floxuridine	Injection	Glass vial	X		A
Fluorouracil	Injection	Glass vial	X		A, B
Flupentixol decanoate	Injection	Glass ampoule	X		B
Fluphenazine HCl	Injection	Glass vial	X		A
Folic Acid	Injection	Glass vial	X		A
Furosemide	Injection	Glass vial/ampoule	X		A, B
Gallamine triethiodide	Injection	Glass vial	X		A
Haloperidol	Injection	Coloured glass ampoule	X		A, B



# Informácie od výrobcu

## HBM

- výrobca Furosemid Forte - nemajú skúšky fotostability
- stabilné max 1 hodinu
- „HBM nemá vykonané fotostability na požadovanú dobu 7 hodín, preto je potrebné používať hnedé hadičky, resp. hadičky chránené pred svetlom.“

- 
- Nepoužívať v prítomnosti nečistôt a pri žltom sfarbení
  - Kontinuálna infúzia dlhšie ako 1 hodinu - fotoprotekcia

# Kyselina askorbová

## SPC

- Uchovávať chránené pred svetlom
- Žiadne informácie o administrácii

## Stabilis

- Skúšky bez prítomnosti svetla

# Stabilita

- Koncentrácie 30/ 50/ 92 mg/ml
- Fyziologický roztok alebo dextróza 5% vo vode, 50 ml
- Chránená pred svetlom – dlhšia stabilita
- Nízka teplota (4°C) – dlhšia stabilita

Stabilná 75 hodín pri 25 °C za svetla

# Kyselina askorbová v parenterálnej výžive

- Zabraňuje peroxidácii lipidov
- Oxidácia na dehydroaskorbovú kyselinu
- Často kvôli stopovým prvkom – hlavne meď, železo
  
- Vyhnúť sa súbežnému zmiešaniu so stopovými prvkami
- Stabilita nezávisle od fotoprotekcie
- Často rozklad kvôli kyslíku prepustenému cez vak/vo vaku pri plnení

- Vo fyziologickom roztoku pri 25°C za svetla – stabilná 75 hodín
- V parenterálnej výžive je stabilná počas 48h pri 25°C

# Zdroje

- Sánchez-Quiles I. et al., Review of the stability of photosensitive medications, *Farmacia Hospitalaria*, 2010, 35(4), 204-215
- Baertschi S.W. et al., Implications of In-Use Photostability: Proposed Guidance for Photostability Testing and Labeling to Support the Administration of Photosensitive Pharmaceutical Products, Part 1: Drug Products Administered by Injection, *Pharmaceutical Sciences*, 2013, 102(11), 3888-3899
- Ahmad I. et al., Photostability and Photostabilization of Drugs and Drug Products, *Int J Photoenergy*, 2016, dostupné z: <http://dx.doi.org/10.1155/2016/8135608>
- Handbook on injectable drugs, 20th edition, ASHP, 2018, ISBN: 978-1-58528-615-7
- Stabilis – dostupné z: <https://www.stabilis.org/index.php?codeLangue=CZ-cz>

- Tonnesen H.H. et al., Formulation and stability testing of photolabile drugs, *Int J Pharm*, 2001, 225, 1-14
- Walker S.E. et al., Administration of Intravenous Ascorbic Acid—Practical Considerations for Clinicians, *Nutrients*, 2019, 11, 2-12, doi:10.3390/nu11091994
- Muhlebach S. et al., Practical handling of AIO admixtures—Guidelines on Parenteral Nutrition, Chapter 10, 2009, 7, ISSN 1612-3174
- SPC Acidum ascorbicum, cit. [23-10-2019], dostupné z: [https://www.sukl.sk/hlavna-stranka/slovenska-verzia/pomocne-stranky/detail-lieku?page\\_id=386&lie\\_id=24836](https://www.sukl.sk/hlavna-stranka/slovenska-verzia/pomocne-stranky/detail-lieku?page_id=386&lie_id=24836)
- SPC Furosemid forte, cit. [23-10-2019], dostupné z: [https://www.sukl.sk/hlavna-stranka/slovenska-verzia/pomocne-stranky/detail-lieku?page\\_id=386&lie\\_id=99333](https://www.sukl.sk/hlavna-stranka/slovenska-verzia/pomocne-stranky/detail-lieku?page_id=386&lie_id=99333)
- SPC Furosemid, cit. [23-10-2019], dostupné z: [https://www.sukl.sk/hlavna-stranka/slovenska-verzia/pomocne-stranky/detail-lieku?page\\_id=386&lie\\_id=43531](https://www.sukl.sk/hlavna-stranka/slovenska-verzia/pomocne-stranky/detail-lieku?page_id=386&lie_id=43531)





Ďakujem za pozornosť