Supportive Care in Cancer

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Internal Medicine, Block 4 5th year students





Supportive care in oncology

- Antiemesis
- Treatment of cancer pain
- Management of hematological toxicity
- Infectious complications
- Metabolic complications
- Nutrition support
- Psychosocial support





Antiemesis

Chemotherapy Induced Nausea and Vomiting CINV



Types of CINV

CINV type	Description
Acute	0-24 h
Delayed	25-120 h (Day 2-5)
Anticipated	prior further chemo cycle
Breakthrough	despite prophylaxis
Refractory	not responding to treatment



Risk factors for CINV

Cytotoxic agents	Patient-based factors
Emetogenic drug	Young age < 50 yr
Higher dose of the drug	Female gender
Combination of drugs	History of vomiting
	CINV after prior chemo cycle
	Anxiosity
	Alcohol abstinence

Classification of cytotoxic drug emetogenicity

Classes of emetogenicity	Probability of CINV without prophylaxis
High	> 90 %
Moderate	30-90 %
Low	10-30 %
Minimal	< 10 %

Generaly emetogenic means the risk of CINV > 30 %



Antiemetic drugs

Class	Generic names	Half life hours
5HT ₃ R inhibitors	ondansetron granisetron palonosetron	3 9 40
NK ₁ R inhibitors	aprepitant netupitant rolapitant	9 96 120
Corticosteroids	dexametasone	
Atypical antipsychotic	olanzapin	
Prokinetic agents	metoclopramide	
Anxiolytics	alprazolam Iorazepam	

Rules for antiemetic prophylaxis

in chemotherapy treated patients

Prevention from the 1st cycle

in emetogenic chemotherapy (moderate to high risk)

Use of full defined doses af antiemetics do not reduce the dose

Combined antiemesis recommended

- dexamethasone is a routine part of combination
- add anxiolytics in anxious patients
- monotherapy for low-risk patients
- Oral formulation sufficient for prevention
- Modern antiemetics with long half life
 potencially 1 dose for the whole cycle of chemotherapy



Combined antiemetic prophylaxis

regimens used according to total CINV risk of the patient

Routine 2-drug regimen for moderate risk patients

5HT ₃ -inhibitor	dexamethasone	
5HT ₃ -inhibitor	dexamethasone	alprazolam

Three drug regimen for high risk of CINV

5HT ₃ -inhibitor	NK ₁ -inhibitor	dexamethasone	
5HT ₃ -inhibitor	NK ₁ -inhibitor	dexamethasone	alprazolam

Olanzapin regimen as an alternative

palonosetron	olanzapin	dexamethasone
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Potencial regimen for the highest emetic risk / after failure

palonosetron	NK ₁ -inhibitor	olanzapin	dexametha
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Akynzeo[©] capsules

netupitant 300 mg / palonosetron 0.5 mg

First fixed 2-drug combination

- both components with long half life
- Inhibits two main pathways of emesis after CT
 - covers both acute and delayed period, highly effective
- 1 capsule 1 hr prior to the start of CT
 - effective for the whole cycle

Improves compliance with antiemetic regimen

- solves known gaps between guidelines and reality
- decreases the risk of mistake
- Cost-effective despite of high charges





Cancer pain management principles of therapy



Chronic cancer pain characteristics

two patterns: continuous or intermittent

Multidimensional phenomen

- complex interaction between many factors
- includes psychological factors
- causes syndrome (rather than symptome in acute pain)

Chronic pain may be a patogen itself

- can facilitate progression of metastatic disease
- negative predictor of survival
- worsens quality of life

Neuropathic pain

- damage to the nerves and surrounding tissues
- pathological persisting type of pain, hyperesthesia
- maladaptive response



Principles of cancer pain management

Drug therapy is the cornerstone

- Prescription on an around-the-clock basis
 - using analgesic ladder
 - use combinations of analgesic drugs
- Strong opioids for increasing and moderate to severe pain
- Specific treatment for neuropathic pain
 - antiepileptics, anticonvulsants
- Rescue doses for breakthrough pain
 - rapidly acting formulations



Analgesic ladder

for cancer pain management

STEP 1

Non opioid analgetics

- paracetamol

Adjuvant (co-analgetics)

- antidepresants, anxiolytics
- anticonvulsants, gabapentinoids
- corticosteroids
- cannabinoids

STEP 2

Weak opioids (+- non-opioid / adjuvant)

STEP 3

Strong opioids (+- non-opioid / adjuvant)



Weak opioids

for cancer pain

Tramadol

- injection i.v., i.m., s.c.
- oral drops, short acting, dosed by 4-6 hrs
- oral slow-release tablets, dosed bid
- combined with paracetamol in tablets

Codein

- short-acting, dosed by 4-6 hrs

Dihydrocodein

- DHC Continus prolonged release tablets, dosed bid
- Oxycodon low dose



Strong opioids

for cancer pain management

Morphine

- injection s.c., i.m.
- oral immediate-release morphine (bioavailability 20-40 %)
- slow-release tablets / capsules, dosed bid

Fentanyl

- TD patch (transdermal), be changed by 72 hrs
- buccal tablets (rapid resorption) for breakthrough pain
- intranasal spray (very rapid resorption)

Buprenorfin TD

- Hydromorhone oral (dosed bid, by 12 hrs)
- Oxycodone oral (dosed bid, by 12 hrs)



Recommendations for opioid therapy

distinct pharmaco-dynamic differences between individuals

Effective dose is very individual

- no ceiling effect to opioid dosing
- □ side effects are usually limiting

Dose of opioids needs to be titrated

- morphine provide similar pain control as newer opioids
- tolerance and physical dependence is predictable
- different from psychological dependence

Undertreatment is common

 uncontrolled pain may decrease cognition, similar to opioid side-effect (for drivers)

Risk of opioid accumulation in renal failure

buprenorfin kinetics preserved in renal insufficency



Recommendations for opioid therapy

distinct pharmaco-dynamic differences between individuals

Opioids should be combined with

non-opioids (paracetamol, NSAIDs)
 adjuvant drugs (antidepressants and others)

Opioid rotation

 switch to different opioid in case of tolerance or side effects to improve effect and/or lower risk of toxicity
 equianalgesic dose caculation

Prophylactic laxatives

useful for many patients (allow opioid continuation)
 combination of opioid with oral naloxone

Use of multiple opioids simultaneosly is inappropriate



Dose-limiting side effects of strong opioids

no defined maximal doses for strong opioids

Respiratory depression

 risk is minimal in adequate dose titration

 Constipation and dry mouth

 independent of dose

 Nausea and vomiting

 usually transient, resolve within days
 Sedation, cloopiness, dizzinios

- Sedation, sleepiness, dizzinies
- Delirium, confusion

dose-limiting side-effect

Cutaneous pruritus





Febrile neutropenia Management of sepsis



Febrile neutropenia (FN)

severe neutropenia increases the risk of infection

Fever	+	Neutropenia
> 38.5 °C		< 0.5 *10 ⁹ /L
> 38.0 °C > 1 hr		severe neutropenia

Not in all FN cases there is an infection.

Criteria of FN may be fulfilled in other causes of fever, like drug fever etc, but infection cannot be excluded in limited time.

Treatment should cover potential causes of infection (risk of rapid progression of infection within hours).



Different risks of febrile neutropenia

fufilling one or more characteristic features

High risk

hematological patients (leukemia)

- expected to continue for more than 5 days
- □ very severe neutropenia < 0.1 *10⁹/L

Hospital stay, i.v. broad spectrum antibiotics

Low risk

- solid cancer patients
- short period of neutropenia < 5 days</p>
- not very severe (above 0.1 *10⁹/L)

Outpatient, oral antibiotics



Empirical antibiotic therapy

in high-risk febrile neutropenia and sepsis

Start immediately after diagnosis

up to 1 hr after diagnosis
 just after collection of blood for culture (2 sets)

Broad spectrum antibiotics i.v.

I full dose recommended for severe infection

cefepime + amikacin

1st choice in this dept

add vancomycin if indicated

risk of G+ infection

meropenem + vancomycin

in hemodynamic instability



Antifungal therapy

in high risk febrile neutropenia and sepsis

Empirical antifungals

- in high risk FN
- persisting fever despite empirical antibiotics day 5-7
- progressive signs of infection

caspofungin or micafungin

Echinocandin class

Treatment of possible/probable fungal infection

- high-resolution CT of lungs (hallo sign)
- dynamic increase in serum galactomannan
 - suspicion for ivasive pulmonary aspergillosis

voriconazole

Azole antifungal class



Diagnosis of sepsis

positive blood culture not required

Infection + SIRS

Documented

- microbiologically
 - blood stream infection
 - urinary tract infection
- clinically
 - pneumonia
 - soft tissue infection

- Fever / hypothermia > 38.3°C / < 36°C</p>
- Tachycardia > 90/min.
 - in fever >100/min.
- Tachypnea > 20 bpm
 - − pCO₂ < 4.2 kPa</p>
- Leukocytosis
 - or leucopenia



Primary site of infection in sepsis 14,364 patients, 28 ICUs, 8 countries





Sepsis continuum

in disease progression





Diagnosis of severe sepsis

require signs of tissue hypoperfusion

Hypotensis responsive to i.v. hydration

- systolic arterial pressure < 90 mmHg</p>
- mean arterial pressure, MAP < 65 mmHg

Serum lactate > 4 mmol/L

- normal range 0-2
- partially depending on liver function

Organ dysfunction

- kidney funcion: oliguria < 0.5 ml/kg/hr (< 100 ml/3 hr)</p>
- lung funcion: hypoxia, dyspnea
- central nervous system: delirium, somnolence, confusion



Diagnosis of septic shock

definition

Sepsis induced hypotension, persisting after i.v. hydration

initial hydration at least 30 mL/kg for 3 hrs
 2100 mL for 70 kg person in 3 hrs

The goal in lactate elevation is to decrease lactate level (improve tissue perfussion)

Vasopressors necessary for septic shock

- norepinephrin is the first choice
- \square MAP > 65 mmHg is the goal







Metabolic complications in oncology



Tumor lysis syndrome, TLS

characteristics

Aggresive malignancy

- Burkitt lymphoma
- acute leukemia
- many other aggresive/chemosensitive tumors

Bulky disease (large tumor volume)

high lactate-dehydrogenase (LD)

Clinical situations

- mosty occurs after first doses of chemotherapy
- chemosensitive malignancies
- even after corticosteroids (ALL, high-grade lymphoma)
- rarely spontaneous TLS



Diagnosis of TLS

laboratory monitoring

Hyperuricemia

- uric acid is final metabolite of nucleic acids
- uric acid precipitation in (in low pH)

Renal failure

- rapid onset within hours

Hyperkalemia

- may rapidly increase from morning to evening
- bradyarrythmia, heart arrest, sudden death
- Hyperphosphatemia
 - calcium phosphate precipitation (in high pH)
- Hypocalcemia



Prevention of TLS

before starting chemotherapy

Prehydration

- start at least 12 hrs before
- 3-6 L/day (oraly + intravenously)
- high urine output (> 100 mL/hr) prior to chemo
- combined with furosemide in older/cardiac patients

Allopurinol pretreatment

- start 24 hrs before starting chemo
- 300-600 mg/day (reduction in renal insufficiency)
- does not treat preexisting hyperuricemia
- risk of drug-drug interactions
- risk of xanthine nephropathy



Urate oxidase enzyme in TLS

rasburicase, recombinant urate-oxidase

Conversion of uric acid to allantoin

10times more soluble than uric acid

Reduces preexisting hyperuricemia

in contrast to allopurinol

Rasburicase i.v. infusion

- plasma uric acid level rapidly decreases within 4 hrs
- single dose 6 mg commonly sufficient
- repeat as necessary
- risk of anaphylaxis (< 1 %)



Monitoring of TLS

according to the risk

Twice daily in patients at high risk

- diuresis (goal > 100 mL/hr)
- biochemistry (kreatinin, K, P, Ca)

Asymptomatic hypocalcemia should not be treated

- risk of calcium-phosphate precipitation
- alcaliniaition of urine not recommended


Hypercalcemia in malignancy

characteristics

Pathophysiology in oncology

- osteolytic metastases (osteoclast activity)
- parathormone-related protein produced by cancer

Symptoms

- osmotic diuresis causing dehydration
- anorexia, nausea, vomiting
- constipation, sometimes severe
- confusion, central nervous system dysfunction



Treatment of hypercalcemia

in malignancy at ICU

Intravenous hydration

- □ saline infusion 200-300 mL/hr
- hypovolemia exacerbates hypercalcemia

Calcitonin

rapidly acting in 4-6 hrs, tachyphylaxis after 48 hrs

Bisphosphonates (more potent than calcitonin)

- zoledronate, pamidronate
- maximal effect in 48-96 hrs (2-4 days)
- potential nephrotoxicity
- used up to kreatinin 400 umol/L

Disease-specific approach

treatment of underlying disease



SIADH in oncology

Syndrome of inappropriate ADH secretion

Pathophysiology

- ADH caused water retention (usually mild)
- secondary increase of natriuresis (natriuretic hormones)
- euvolemic hyponatremia

Laboratory abnormalities

- hyponatremia (may be asymptomatic)
- low plasma osmolality (hypoosmolar hyponatremia)
- urine Na concentration > 20 mmol/L (natriuresis)

Clinical features

- asymptomatic hyponatremia is a common feature
- apetite loss, headache, dizzinies, muscle weakness
- no oedema



Etiology of SIADH in oncology

Underlying cancer

- lung cancer (SCLC)
- mesothelioma
- oropharyngeal, gastric, pancreatic cancer
- malignant lymphoma

Drugs as a side effect

- antidepressants (mainly SSRI)
- antiepileptics
- antipsychotic agents
- cyclophosphamide, ifosfamide, vincristin



Treatment of SIADH

Water restriction

 $\hfill\square$ to 800-1000 mL daily

Furosemide

eliminates more water than sodium

Sodium chloride infusion

normal saline (0.9 % solution)
 slow gradual correction of natremia
 not faster than by 0.5-1 mmol Na in 1 hour
 rarely hypertonic saline (3% solution)

Vasopresin receptor antagonists
 acting on renal tubuli blocking V₂R





Nutrition support in cancer



Diagnosis of malnutrition

is based on simple clinical findings

Unwanted weight loss > 10 % per 6 months

- prognostically different from weight reduction
- also applies to overweight and obese patients

Decreased BMI

- interpretation depends on age and gender

Insufficient food intake

less than 60 % of usual intake more than 10 days

Nutrition impact symptoms

increase risk and probability of reduced food intake

Serum albumin is not a reliable marker



Median overall survival in cancer patients

in months, according to baseline weight loss and BMI n=8160

11-0100	BMI 28 25 22 20					
WL	21.5	19.9	15.7	13.5	8.4	17.3
2.5 %	14.2	11.9	10.5	10.6	7.8	11.3
6 %	10.7	9.2	6.8	6.7	4.7	7.5
11 %	8.1	8.1	6.2	5.4	4.4	6.2
15 %	7.1	4.8	4.7	3.7	4.1	4.4
	13.1	10.2	8.1	6.1	4.7	



Martin L...Baracos V. J Clin Oncol 2015; 33:90-99.

Grading of weight loss in cancer patients worsening prognosis through grades 1-4



 $\sum_{i=1}^{n}$

Martin L...Baracos V. J Clin Oncol 2015; 33:90-99.

Median overall survival in cancer patients by grading of weight loss, n=8160



Martin L ... Baracos V. J Clin Oncol 2015; 33:90-99.



Interpretation of BMI for diagnosis of underweight

low BMI alone should not be classified as malnutrition

	Age 18-25 <i>yr</i>	Age 25-65 <i>roků</i>	Age > 65 roků
BMI muži	19.0	20.5	22.0
BMI ženy	18.5	20.0	22.0

Example: BMI below 22 kg/m2 in seniors is in the range of underweigt and may support the diagnosis of malnutrition



High correlation of Mid Arm Circumference, MAC with BMI, n=1561



Change of 1 BMI unit (3 kg for 173 cm height) reflects 1 cm of MAC

3 mm change of MAC reflects change 1 kg in body weight

Applies to mid stature 173 cm $(1.73^2 = 3,0)$

There is approx. 5 unit difference between MAC and BMI



Powell-Tuck, Hennessy, Clinical Nutrition 2003, str.307-312

Mid Arm Circumferencer, MAC

cut-off values for diagnosis of malnutrition

OP	Normal (median) cm	Mild malnutrition cm	Severe malnutrition cm
Males	31.0	26.0	23.0
Females	30.0	25.0	22.0

Applies to mid stature around 173 cm. Excellent parameter in fluid retention, edema, ascites.



Cancer cachexia

is characterized by metabolic abnormalities with systemic inflammation in many, but not all patients, progressive loss of skeletal muscle mass is crucial

Weight loss < 5%	> 5-10 %	> 20-30 % > 30 %
Precachexia	Cachexia	Refractory cachexia
Early metabolic changes IL-6↑ CRP↑ albumin↓	Systemic inflammation Anorexia	Performance status↓ Survival < 3 mo

Glasgow Prognostic Score, GPS, range 0-2 points

CRP > 10 mg/L Albumin < 35 g/L Score 1-2 points (in the absence of infection) reflects systemic inflammation, cancer cachexi and poor prognosis

Muscle area by CT at L3 level enables calculation of total body muscle mass



Total energy requirements in cancer patients

Common low physical activity	25-30 kcal/kg/Day
	1.4 * BEE
Higher physical activity mostly younger pts. and males	30-35 kcal/kg/Day
	1.5 * BEE
Malnutrition, after weight loss mostly younger pts. and males	35-40 kcal/kg/Day
	1.6 * BEE

Expression per kilo BW applies to normal weight patients (normal BMI). Corrected weight is used for overweight and underweight (to the middle between Ideal BW (BMI 22 for mid age, 24 for seniors) and Actual BW.

Protein requirements in cancer patients

delivery of increased needs in cancer is safe

Mild / moderte malnutrition	1.2-1.5 g/kg/Day
Severe malnutrition	1.5-2.0 g/kg/Day
Renal isufficiency	1.0-1.2 g/kg/Day

Expression per kilo BW applies to normal weight patients (normal BMI). Corrected weight is used for overweight and underweight (to the middle between Ideal BW (BMI 22 for mid age, 24 for seniors) and Actual BW.



Dietary counselling

in cancer patient with anorexia/nausea

- Releive unnecessary dietary restrictions
- Treat nutrition impact symptoms
 - pain, nausea, anorexia, diarhea, constipation
- Eat small portions 5-6 times a day
- Keep variety of foods
- Take energy dense foods
 - increase fat intake
- Increase protein intake
- Easy access to food snacks
- Attractive serving of meals



Oral Nutritional Supplements, ONS

ready to use for sipping, 125-300 mL/can

Complete formulas for oral intake

- high content of energy, proteins, vitamines
- specific composition (omega-3 fatty acids)
- Liquid or creme consistency
- Cans 125 ml, 200 ml, 220 ml, 300 ml
- Many different tastes
- Easy used in dental and swallowing problems
- Easily digestable
- Success with ONS depends on adequate motivation and individual approach



Classification of ONS

Category	Characteristic
High Protein	20 g proteins / can
High Energy	2 kcal / mL
Small volume	125 ml, concentrated up to 3.2 kcal / ml
Large volume	300 ml, up to 600 kcal / can
Diabetic formula	low glycemic index
Omega-3 PUFA	0.75-1 g EPA / can
Muscle support	HMB, high protein / vitamin D





Fine bore NG tube

introduced by guidewire for nasogastric feeding

Importance of fixation to face

Polyuretan material for use up to 3 months



Percutaneous endoscopic gastrostomy, PEG



Classification of products for tube feeding

Category	Characteristic	Signed
Standard	1.0 kcal / mL	Standard
Energy	1.5 kcal / mL (2 kcal / mL) 1500-2000 kcal / 1 L	Energy
High Protein	75-100 g proteins / 1 L	HP
Containing fibre	15 g fibre / 1L	Fibre
Diabetic formula	low glycemic index contains soluble fibre	Dia-, Dib- Glu-
Omega-3 PUFA	2 g EPA / daily dose of energy	
Muscle support	hydroxy-methyl-butyrate, HMB high protein and vitamin D	

Total parenteral nutrition (TPN)

in cancer patients

- Enteral nutrition cannot be used
 - bowel obstruction and other contrasindications
- Survival is more limited by malnutrition than progression of cancer
- Life expectancy > 3 months
 - only patients surviving more than 2 mo profit from PN
- Performance status KPSI > 50, ECOG 0-2
 ability to walk even upstairs
- Family consensus, good background
- Start only after meticulous deliberation
 - decision should not come from despair
 - PN should not prolong suffering



Supplemental parenteral nutrition, Suppl PN

new modality of nutrition support in cancer patients

Potential indication

- Insufficient food intake
 - inability to deliver more nutrients through GI tract
 signs of malabsorption (diarrhea)

Continuing weight loss despite oral nutritional intervention with ONS

- Malnutrition has not been severe so far
- Advanced cancer, but death is not imminent
 cancer is not rapidly progressive
- For multimodal paliative care



Advantages of supplemental PN

Partially preserved enteral intake Supporting bowel function

Lower amount of i.v. nutrients

- lower side effects (hyperglycemia etc.)
- Iower risk of canulla infection
- shorter time of delivery

Patient need not take PN each day

- depending on oral intake and body weight
 free days from PN
- Helps to keep body weight / muscle mass
- Improvement of Quality of Life



PICC, Peripherally Inserted Central Catheter tip of catether in superior vena cava





Nutriflex Omega Special 1250 ml

3-chamber bag

1475 kcal 6100 kJ

Aminoacids 70 gGlucose180 gFat50 gEPA+DHA 3.1 g



SMOF Kabiven 986 ml for supplemental PN



1100 kcal 4600 kJ AA 50 g Glucose 125 g Fat 38 g **4-component** fat emulsion S soya MCT Μ oliv oil 0 F fish oil

Content



Preparation of "All in one" admixture in hospital pharmacy



Rodné č.: 986209/ Jméno: Gráfová P Odd.: IHOK ASEPT.	avla	Č. objedn.: Objem (ml): míška	10 684 1 620
Neonutrin 15%	700.0 ml		
Glukóza 40%	500.0 ml		
Smoflipid 20%	350.0 ml		
KCI 7,45%	20.0 ml		
KH2PO4 13.6%	20,0 ml		
Ca gluconicum 10%	20.0 ml		
MgSO4 10%	10,0 ml		
Složení vaku:			
Calcium [mmol]:	4,5	Natrium [mmol]:	0,0
H2PO4 [mmol]:	20,0	Chloride [mmol]:	20,0
Magnesium [mmol]:	4,1	P org. [mmol]	0,0
Kallum [mmol]:	40,0		
Obsah dusíku [g]:	15,6	Osmol. [mOsm/l]:	1 296,6
Cukry [g]:	200,0	Energie [kcal]:	1 897,6
Tuky [g]:	70,0	Konc. M+ [mmol/l]:	24,7
Bílkoviny [g]:	104,3	Konc. M++ [mmol/l]:	5,3
*** PODAT	POLIZE DO	Ο ΓΕΝΤΒΑΊ ΝΙ ΖΊΙ Υ **	< *



Lékárna FN BRNO, Jihlavská 20, Brno 62500

700.0 ml

500.0 ml

350.0 ml

20.0 ml

20.0 ml

20.0 ml

10.0 ml

4,5

20,0

4,1

40,0

15,6

70,0

104.3

Uchovávat při teplotě +2 °C až +8 °C, chránit před světlem

gr. Jana Pečivová Datum přípravy: 25.6.2018 Použitelné do: 2.7.2018

Potřeba ručně přidat složky:

200,0

Č. objedn.: 10 684

1 620

0,0

20,0

0,0

1 296,6

1 897.6

24.7

Objem (ml):

Natrium [mmol]:

Chloride [mmol]

Osmol. [mOsm/l]

Konc. M+ [mmol/l]

Konc. M++ [mmol/]

Porg. [mmol]

Energie [kcal]:

DAT POUZE DO CENTRÁLNÍ ŽÍLY *** Připravil: Burianová Kontroloval: De Pe

Rodné č.: 986209/4594

Jméno: Gráfová Pavla Odd.: IHOK ASEPT.J, Mudr. Tomíška

Glukóza 40%

Smoflipid 20%

KH2PO4 13.6%

Složení vaku: Calcium [mmol]

H2PO4 [mmol]:

Kalium [mmol]:

Cukry [g]:

Tuky [g]:

Vytvořil:

Bilkoviny [g]:

Obsah dusíku [g]:

Magnesium [mmol]:

Ca gluconicum 10%

KCI 7.45%

MgSO4 10%

Připravil: Burianová

Kontrolovalena Pečivová

Vytvořil: Mgr. Jana Pečivová

Datum přípravy: 25.6.2018 Použitelné do: 2.7.2018 Uchovávat při teplotě +2 °C až +8 °C, chránit před světlem Potřeba ručně přidat složky:

AiO bag, individualized dose of nutrients for 24 hr

New mixture of vitamins Viant[®] contains all 13 vitamins

Vitamin		Unit	Requirement iv.	Viant lag.
B ₁	Thiamine	mg	6	6
B ₂	Riboflavin	mg	3.6	3.6
B ₃	Nikotinamidum	mg	40	40
B_5	Ac.pantothenicum	mg	15	15
B ₆	Pyridoxin	mg	6	6
B ₇	Biotin	μg	60	60
B ₉	Acidum folicum	μg	600	600
B ₁₂	Cyanokobalamin	μg	5	5
С	Ascorbic acid	mg	200	200

New mixture of vitamins Viant[®] contains all 13 vitamins

Vitamin		Unit	Requirement iv.	Viant lag.
Α	Retinol equivalent	μg	800-1000	1000
D_3	Cholecalciferol	μg	20	5
Е	Tocoferol- α eqival.	mg	10	9.1
K ₁	Phytomenadion	μg	150	150



Nutryelt[®]

new composition contains 9 trace elements

Trace element		Unit	Requirement iv.	Nutryelt
Zn	Zink	mg	3-6.5	10
Se	Selenium	μg	60-100	70
Fe	Iron	mg	1,2	1
Cu	Copper	μg	300-500	300
Mn	Manganese	μg	60-100	55
F	Fluor	μg	950	950
Т	lodine	μg	130	130
Мо	Molybdenum	μg	19	20
Cr	Chromium	μg	10-20	



The end

