ROLE OF CLINICAL PHARMACIST IN PEDIATRIC CANCER CARE

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CANCER CARE 2 DECADES AGO

- CANCER TREATED PRIMARILY BASED ON HISTOLOGY, LOCATION AND SIZE; FEW BIOMARKERS
- APPROXIMATELY 200 FEWER TREATMENT OPTIONS THAN TODAY
- THREE BASIC TREATMENT MODALITIES
- LIMITED SUPPORTIVE CARE OPTIONS

CANCER CARE CONCEPT IN THE 21ST CENTURY

- INDIVIDUAL TAILORED THERAPY
- SYSTEMIC THERAPY
- MORE CURABLE TO CHRONIC STATE
- OLD CONCEPT "DISEASE-FOCUSED APPROACH"
- NEW CONCEPT "PATIENT-FOCUSED APPROACH"
- INTEGRATING OF "SUPPORTIVE CARE"
- PRECISION MEDICINE PRACTICE MODEL

Liekweg A, et al. Support Care Cancer 2004;12:73-79. Walko C, et al. Am J Health-Syst Pharm 2016; 73:1935-1942.

ROLE OF ONCOLOGY PHARMACIST

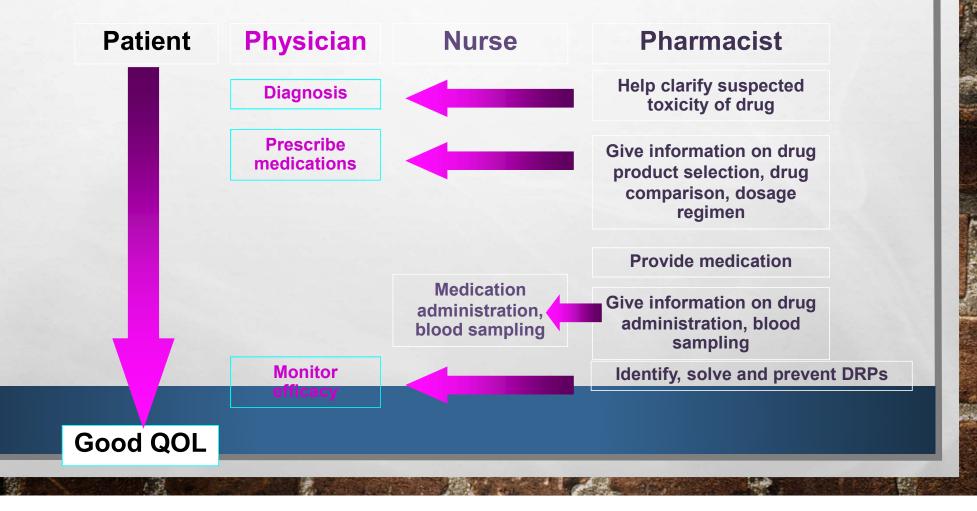
As an integral part of the cancer care team, oncology pharmacists are involved with the care of cancer patients at all phases of their treatment



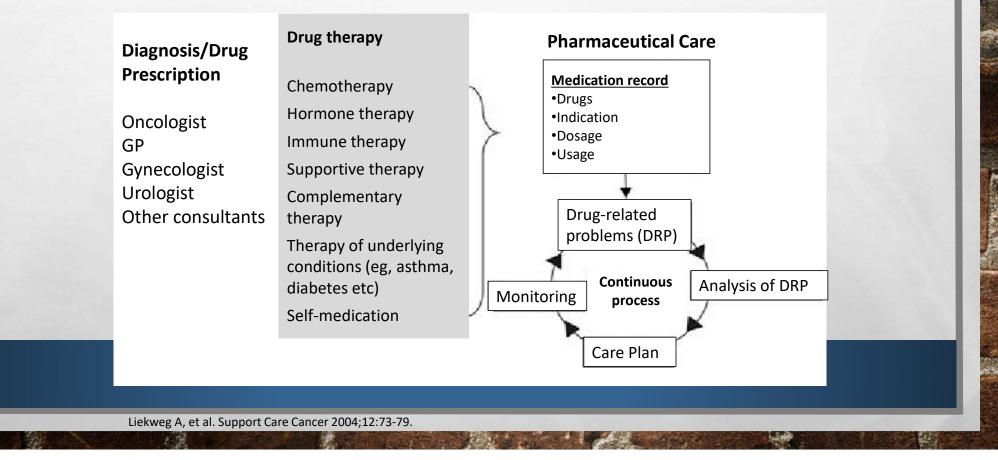
Role of pharmacist in oncology care



DRUG USE PROCESS

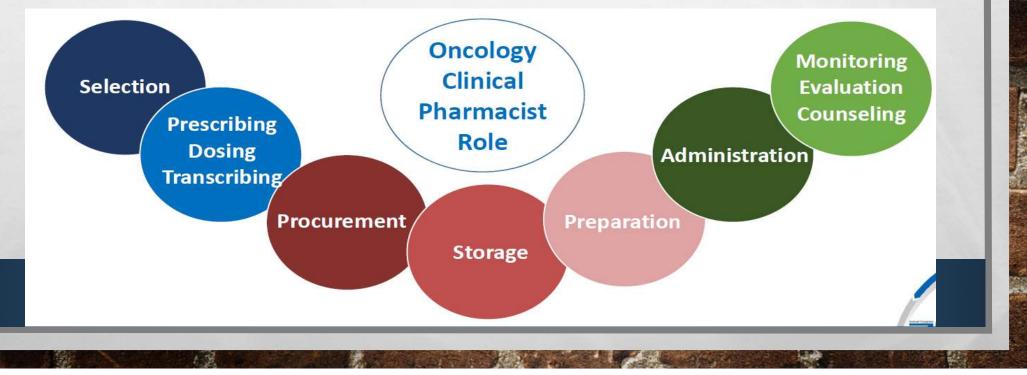


PHARMACEUTICAL CARE IN ONCOLOGY



TREATMENT MANAGEMENT PROCESS

THE JOINT COMMISSION OUTLINES A PROCESS OF 7 CRITICAL STEPS THAT CONSTITUTE SAFE AND COMPLETE MEDICATION MANAGEMENT



1. SELECTION

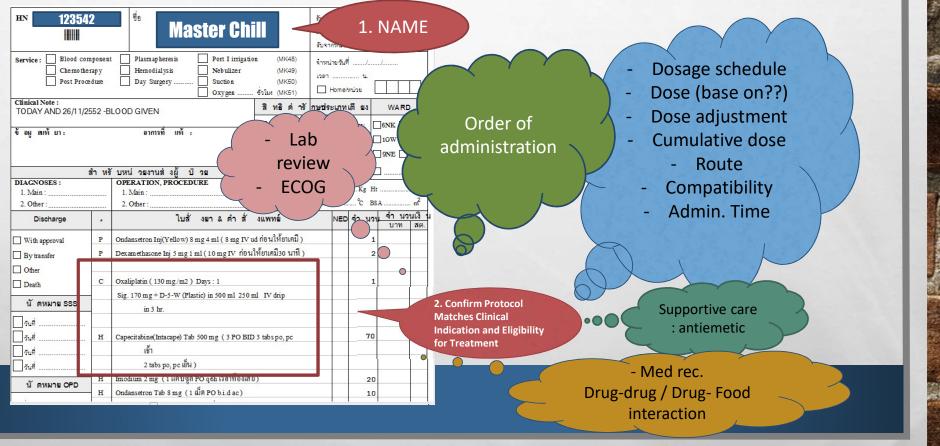
ONCOLOGY CLINICAL PHARMACISTS PROVIDE MEDICAL INFORMATION ABOUT

- ANTINEOPLASTIC PHARMACOLOGY
- DOSING ADJUSTMENTS FOR ORGAN DYSFUNCTION
- ADVERSE-EFFECT PROFILES
- FREQUENTLY ASKED QUESTIONS
 - LITERATURE DOCUMENTING OFF-LABEL USE OF AN ANTICANCER DRUG
- PHARMACOGENOMICS CONSIDERATIONS:
 - EXAMPLES: EGFR INHIBITORS (GEFITINIB, ERLOTINIB, CETUXIMAB) CMT (IRINOTECAN)



2. PRESCRIBING, DOSING AND TRANSCRIBING

Step of CMT order assessment and review



Clinical Note :			สิ <mark>ทธิด่า</mark> รั	กษ <mark>ป</mark> ระเภท	เตียง	WARD	
ข้อมูลแพ้ยา:		อาการที่ แพ้ :	. 🗹 เงินสด 🗌 ต้นลังกัด ประกันสุขภาพ ประกันสังคม	🗌 3 ซม. [6 ซม.	6NK 7NK 10W 20W	
	สำ หรื	รับหน่วยงานส่งผู้ ป่วย	🗌 ประกันชีวิต		ขม.	SDSSS5	
DIAGNOSES :		OPERATION, PROCEDURE	อื่น ๆ ระบุ	wt 56	Kg	Ht 162	
1. Main : 2. Other :		1. Main : 2. Other :		Temp			
Discharge	*	ใบสั่งยา & ดำสั่	งแพทย์	NED	จำ น	1211 án	Drug interaction
With approval	P	DiphenhyDRAmine Capsule 25 mg { Sig. 2 IIF	ปซูล PO ก่อนให้ย	าเคมี30		2	
By transfer		min. }					
Other	P	Ranitidine 50 mg 2 ml { Sig. 1 Amp IV ก่อนให้	เ้ยาเคมี 30 min }			1	
Death	P	Ondansetron Inj(Yellow) 8 mg 4 ml { Sig. 8 mg	IV ud ก่อนให้ยาเค	มี		1	
		30 min.)					
นัดหมาย SSS	P	Dexamethasone Inj 5 mg 1 ml { Sig. 20 mg IV (orn ก่อนให้ยาเคมี	30		4	
วันที่ 10.สี.ค.ธ		นาที }					
วันที่	P	Emend Cap. 125 mg { Sig. 1 เม็ค PO ก่อนให้ย	าเคมี30 min. }			1	
วันที่							
วันที่	С	Intaxel (175 mg/m2) Days : 1			27	75	
นัดหมาย OPD		Sig. 275 mg + NSS (Glass) 500 ml IV IV drip	o in3				Reduce dose of dexamethasone to 12 mg
	-	hr.					neadee dose of dexamethasone to 12 mg
วันที่ / /							
เวลา	н	Metoclopramide Tab 10 mg { Sig. 1 เม็ค t.i.d ac	2}		2	21	
คลินิก	н	Ondansetron Tab 8 mg { Sig. 1 เมื่ด PO b.i.d ac	}			9	
	н	Emend Cap. 80 mg { Sig. 1 เม็ค PO od D2-3 }				2	
แพทย์							

• 8 YR GIRL WITH ALL

SHE CAME TO HOSPITAL FOR RECEIVED CHEMOTHERAPY PHASE II- CONSOLIDATION WK4

Thai Pediatric Oncology Group ชมรม โรคมะเร็งเด็ก

Phase II: PH-CON	SOLIDATION-I (4 weeks)		Date s	tart	
Hospital	HN	BW	Ht	BSA	
Patient's name			Age	Sex	_
				Page	3 of 1

Start Consolidation-I on Day 36 of Induction (7 days following day 29 LP) or when peripheral count

recovery with ANC ≥750 and Plt ≥75,000 whichever occurs later.

Week	1	2	3	4	5
Day	1	8	15	22	29
Date due					
Date given					
Medication:					
CPM mg IV	с				Begin
ARAC mg IV	ÄÄÄÄ	ÄÄÄÄ			Consolidation-II
6-MP mg PO daily					on Day 29 or when
L-ASP IU IM			A	А	CBC parameter
VCR mg IV			v	v	was met
IMAT mg PO daily					whichever occurs
TITmg	т	т	т		later.
Investigation:					
CBC/diff	+	+	+	+	
CSF cell count/ cytospin	+	+	+		
BUN, Cr, TB,DB, AST, ALT	+				

Drug		Do	sage		Days
Cyclophosphamide (CPM)	1,000 mg/m ² /dose IV over 30-60 min				Day 1
Mesna	250 mg/m ² /dose I	250 mg/m ² /dose IV drip in 15 minutes at hr 0, 4, 8, of CPM			
Cytarabine (ARAC)	75 mg/m ² /dose IV over 15-30 min or SC daily				Day 1-4, 8-11
Mercaptopurine (6-MP)	60 mg/m ² /dose P	O daily (hs)			Day 1-14
L-Asparaginase (L-ASP)	25,000 IU/m ² /dose IM			Day 15, 22	
Vincristine (VCR)	1.5 mg/m ² /dose IV	1.5 mg/m ² /dose IV push over 1 min (Max 2 mg)			Day 15, 22
Imatinib (IMAT)	340 mg/m ² /dose PO daily			Day 1-29	
Triple Intrathecal (TIT)	Age (yrs)	MTX: Dose	HDC: dose	Ara-C: dose	Day 1, 8, 15
	1-1.99	8 mg	8 mg	16 mg	
	2-2.99	10 mg	10 mg	20 mg	
	3-8.99	12 mg	12 mg	24 mg	
	≥9 (but <30 kg)	12 mg	12 mg	24 mg	
	≥9	15 mg	15 mg	30 mg	

Note:

 Imatinib should be hold if ANC <750/µL or Plt <75,000/µL on day 29. Repeat CBC weekly until patient is ready to start next phase. Recommend repeat BM aspiration if cytopenia persist more than 3 weeks.

 Trimetroprim-Sulfamethoxazole 150/750 mg/m²/day (Max 320 mg) po bid 3 consective days/week as soon as possible

Consider hydration post L-asparaginase (optional)

VinCRIStine / Itraconazole



Risk Rating

D: Consider therapy modification

Summary

Itraconazole may enhance the adverse/toxic effect of VinCRIStine. Itraconazole may increase the serum concentration of VinCRIStine.

Severity Major

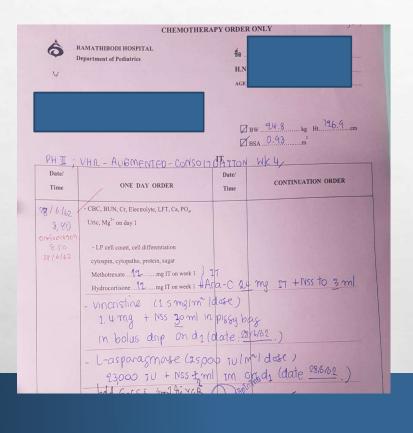
Reliability Fair

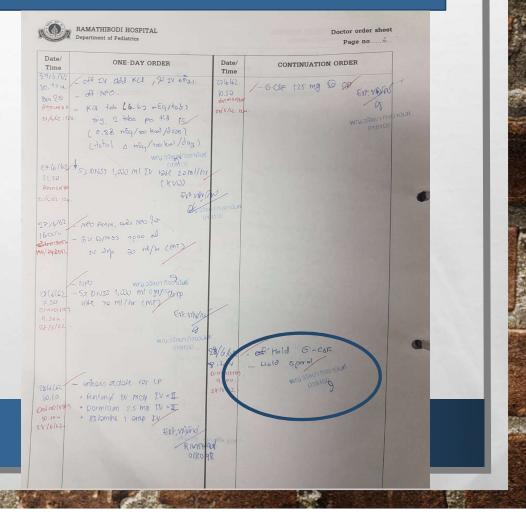
Discussion

Several case reports describe often serious vincristine toxicity (commonly neurotoxicity, gastrointestinal toxicity, and/or myelosuppression) associated with concurrent use of itraconazole.^{1,2,3,4,5,6,7,8,9,10} In two separate in vitro studies, itraconazole restored sensitivity the vinca alkaloid vinblastine among previously-vinblastine resistant cultured cells.^{11,12} In one study, this effect was unique to itraconazole, as ketoconazole, fluconazole, and miconazole were unable to reverse vinblastine resistance.¹¹

The mechanism of this interaction appears to be itraconazole inhibition of vinca alkaloid metabolism (via CYP3A4/5) and/or transport (via p-glycoprotein). Itraconazole is a strong inhibitor of CYP3A and p-glycoprotein, and vincristine is a known CYP3A4/5 substrates.¹³

Drug interaction : Itraconazole vs vincristine





3. PREPARATION





Past: IV PUSH Preparation

NOW: IV PUSH Preparation

3. PREPARATION

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วยพูบ 10	
METHOTREXATEMG	(IT)

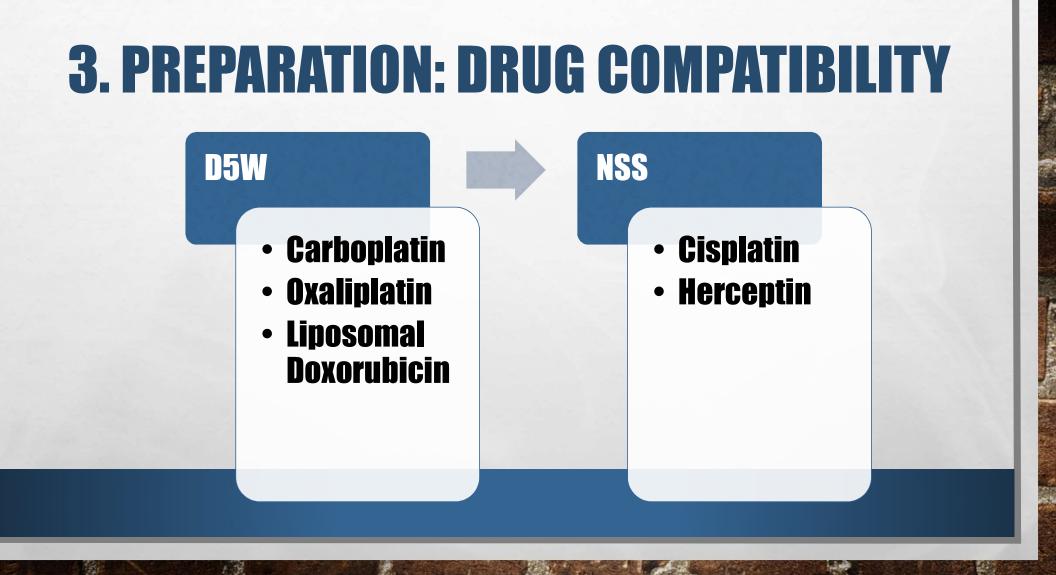
กผู้ป่วย	ປ້າຍ			
n CYTOSARmg + METHOTREXATE	mg +			
TYDROCORTISONEmg in NSSml	(TT)			

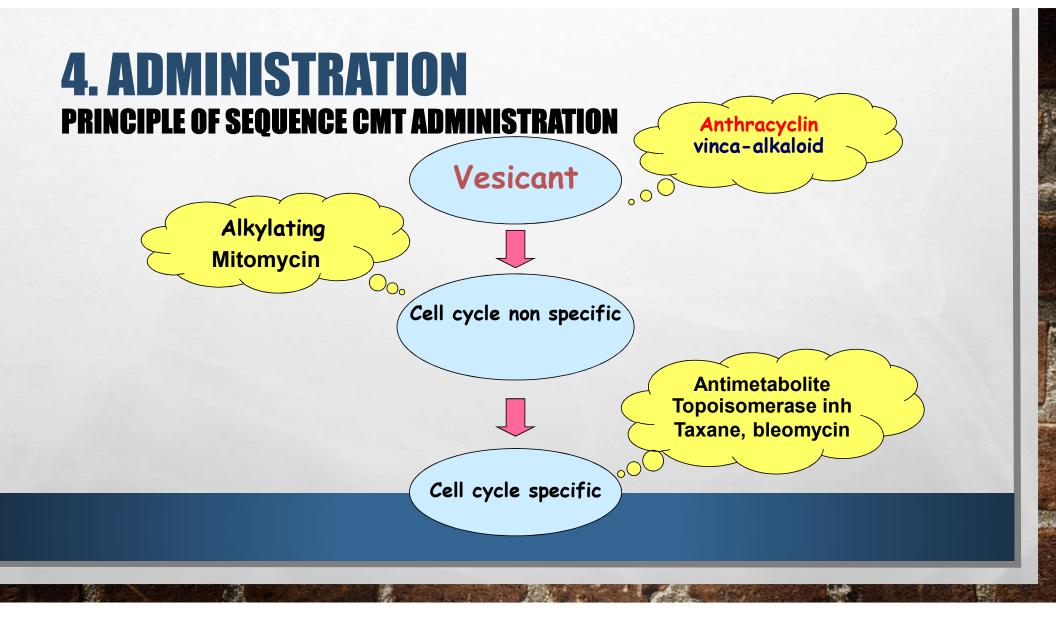
-

3. PREPARATION

• ETOPOSIDE SHOULD BE DILUTED TO CONCENTRATION 0.2-0.4 MG/ML

Orders for 1 day only	Date	Orders for Continuation	Date of
Wt. = 52.8 HT = 174 (M= 185A = 1.54	Hour		Hour .
Conditioning regimen (TICE) Autologouse SCT	- lilia	Diagnosis	
Prehydration Cr> 0.41, GFP : 89	grant oun?	Diet as tolerated	
DEW 1000 co + KC120 - E-1 N 1000 15 E	7- Mg 50 4 2ml	Record BW OD	
x 2 100 IV in 24 hr 100 Day -7 24 hr before		Record V/S, I/O as usual	
chemotherapy w2.4	พาวรรณ เอี่ย		
/	004304	Bed rest if plt < 20,000	
Premedication		Medications	
- Ondansetron 9.30 - 21.30		- Bactrim 2 tab po bid day - 6 to day - 3	
Sig K mg IV at 30 minutes before Etoposide then		(
q 12 hours for breaktrough nausea (Day-6 to -3)		- Acyclovir 400 mg po tid 🗸	
- Dexamethasone & mg IV at 30 minutes before		เริ่ม day - 6 ()	
Etoposide then q 12 hours (Day-6 to -3) 9.30 - 21.	30	- Ranitidine 150 mg po bid	
		เริ่ ม day -6 (
		- Allopurinol 300 mg po OD	
Chemotherapy 1. Carboplatin(700 mg/m ²) = $\frac{1}{2}$, 11°, mg + D5W 1000		193 day - 6 10 -3(-716162 - 101	
		- G-CSF (5ug/kg/d)	
cc IV in 20 hr X 3 days Day -6 to -4 ($\frac{.716167}{10000000000000000000000000000000000$		15 ¹ 11 day + 1 (14/6/62)	Con
	or 1100 My/	- Ondunsation (3)1×2 fac, p - netoclopianide (10) 1×3 6 u	m) ?
2. Etoposide $(280 \text{ mg/m}^2) = .420 \text{ mg} + D5W 1000 \text{ cc}$		- neto dopramide (10) 1×360	())
12 br X 4 days 10 - 22		- olanzapine (5) 1xhs By 71	
$\frac{1}{10} \frac{1}{10} \frac$		- orangapine containt of th	
		٩.(
3. Infuse Stem cell Day 0 () Hydocortisone 100 mg IV 15 min nou Infuse cell	10 10 100	Fumulan on at **Etoposide concentration ≤ 0.4 mg/ml	





CELL CYCLE NON SPECIFIC

Alkylating agent	Platinum : cisplatin carboplatin oxaliplatin Nitrogen mustard : cyclophosphamide ifosfamide Triazenes : dacarbazine	
Anthracycline	Doxorubicin Epirubicin idarubicin Daunorubicin Mitoxanthrone	
Some antibiotics	Mitomycin Dactinomycin	

CELL CYCLE SPECIFIC

Antimetabolite	Folate antagonist : MTX pemetrexed Purine analogues : 6-MP,6-TG,Fludarabine Pyrimide analogues: 5-FU,Ara-C,Gemcitabine
Antimicrotubules	Taxane: paclitaxel docetaxel Vinca: vincristine vinblastine vinorelbine
Topoisomerase I inhibitor	Irinotecan, topotecan
Topoisomerase II inhibitor	etoposide, teniposide
Some antibiotics	bleomycin

SEQUENCE OF CMT ADMINISTRATION

Doxorubicin --> Paclitaxel Paclitaxel --> ×Carboplatin / Cisplatin 5-FU --> MTX Paclitaxel --> Gemcitabine Vinblastine --> Bleomycin

SPECIAL ADMINISTRATION BY NG TUBE

- DISSOLVE THE TABLET IN 100 ML OF WATER WITH RESULTING IN SUSPENSION
- RINSE THE CONTAINER TWICE WITH 40 ML OF WATER



SPECIAL MEDICATION BY NG-TUBE

Avoid crushing tablets

Use the injection to prepare an oral solution

should be undertaken in appropriate facilities

SPECIAL MEDICATION BY NG-TUBE

Cyclophosphamide	 Extemporaneous liquid preparations for oral administration may be prepared by dissolving tablets in aromatic, Elixir. Preparations should be stored under rerigeration in glass containers and used within 14 days
Capecitabine	Fill the cup with 200 ml of water and add the correct number of Capecitabine tablets. Leave the tablets in the liquid to dissolve. This may take about 15 minutes
Temozolamide	mixing Temozolamide capsule with apple juice in chemo hood. [stability =120 minutes when mixed with apple juice or applesauce]

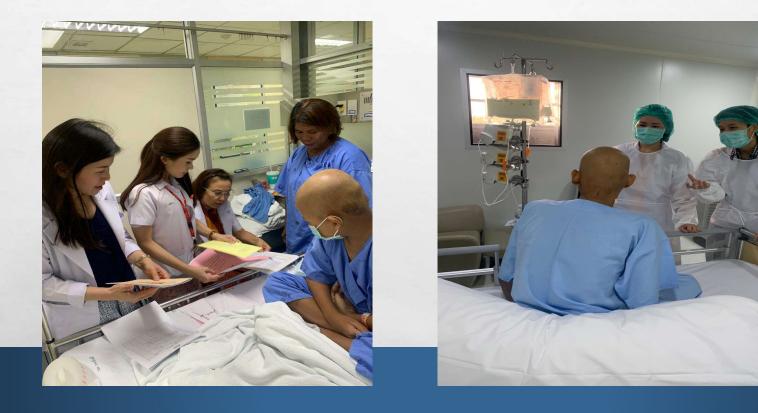
INTRAGASTRIC ADMINISTRATION: CYCLOPHOSPHAMIDE

- STOP THE ENTERAL FEED.
- FLUSH THE ENTERAL FEEDING TUBE WITH THE RECOMMENDED VOLUME OF WATER.
- DRAW THE MEDICATION SOLUTION INTO AN APPROPRIATE SIZE AND TYPE OF SYRINGE.
- FLUSH THE MEDICATION DOSE DOWN THE FEEDING TUBE.
- DRAW AN EQUAL VOLUME OF WATER INTO THE SYRINGE AND ALSO FLUSH THIS VIA THE FEEDING TUBE (THIS WILL RINSE THE SYRINGE AND ENSURE THAT THE TOTAL DOSE IS ADMINISTERED).
- FINALLY, FLUSH WITH THE RECOMMENDED VOLUME OF WATER.
- RE-START THE FEED, UNLESS A PROLONGED BREAK IS REQUIRED

PATIENT EDUCATION MATERIAL



5. MONITORING EVALUATION COUNSELING













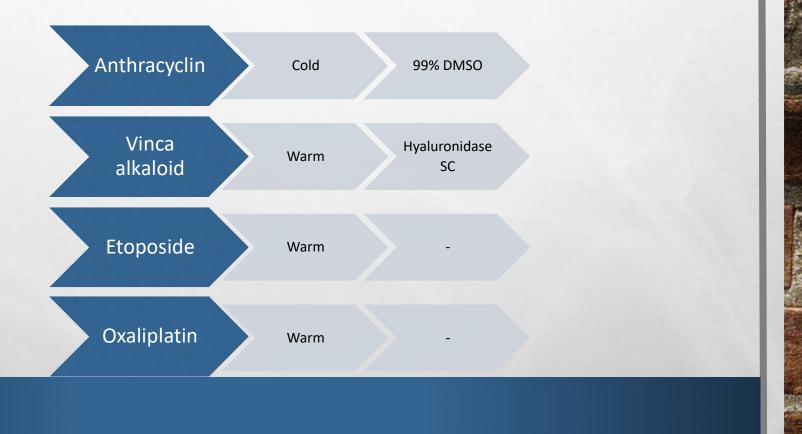
VESICANT DRUG

Anthracycline	Doxorubicin Epirubicin idarubicin
	Daunorubicin
	Mitoxanthrone
Vinca alkaloid	Vincristine Vinblastine Vinorelbine
Some antibiotics	Mitomycin Dactinomycin

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EXTRAVASATION

A S



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EXTRAVASATION : MANAGEMENT

STOP INFUSION

- ASPIRATE ANY DRUG VIA THE IV CANULA
- IF ANTIDOTE IS AVAILABLE INSTILL THROUGH EXISTING IV PRIOR TO REMOVAL
- REMOVE THE CATHETER
- COLD/WARM COMPRESS + ANTIDOTE
 - 15 MINS 4 TIMES A DAY X 3 DAYS
 - DMSO 15 ML Q 6 HR X 7-14 DAYS

EXTRAVASATION MANAGEMENT

Fidalgo J.A. Perez, et al. Annals of Oncology 2012; 23(7):vii167-vii173.

Step 1. Stop and disconnect infusion. Leave the needle in place.

> Step 2. Identify extravasated agent.

> > Step 3.

Leaving the cannula in place, try to gently aspirate as much extravasated solution as possible. Record volume removed in patient records. Avoid manual pressure over the extravasated area. Remove cannula.

Step 4.

Mark with a pen an outline of the extravasated area.

Step 5.

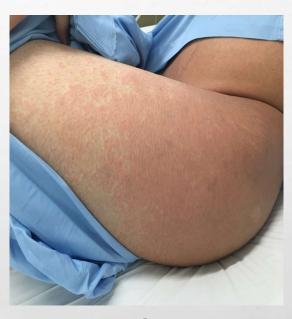
Notify physician. Start specific measures as soon as possible.

Localize and neutralize Agents: - Anthracyclines - Antibiotics (Mitomycin / Dactinomycin) - Alkylating agents	Disperse and dilute Agents: - Vinka alkaloids - Taxanes - Platin salts	Local dry cold compresses
Step 5.A: Localize pply dry cold compresses for 20 inutes 4 times daily for 1-2 days. Avoid alcohol compresses	Step 5.A: Disperse Apply dry warm compresses for 20 minutes 4 times daily for 1-2 days	
Step 5.8: Neutralize Use specific antidotes Antracyclines Topical DMSO Dexrazosane Mitomycin C	Step 5.B: Dilute Administer agents increasing resorption Vinka alkaloids and Taxanes Hyaluronidase	
Topical DMSO		

Elevate the limb. Administer analgesia if necessary.

ADR MONITORING





Infusion reaction from ATG

ADR MONITORING



SEVERITY EVALUATION

Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0

Published: November 27, 2017

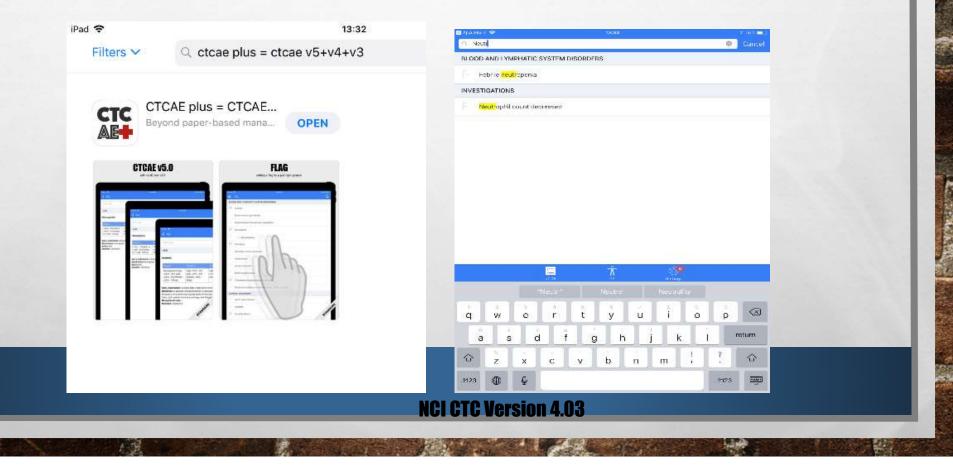
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute

https://ctep.cancer.gov/protocolDevelopment/electronic applications/docs/CTCAE v5 Quick Reference 8.5x11.pdf

DEFINITION AND GRADING



CONTENT OF PATIENT COUNSELING: *ASHP GUIDELINES*

- 1. THE MEDICATION'S TRADE NAME, GENERIC NAME
- 2. THE MEDICATION'S USE, EXPECTED BENEFITS AND ACTION
- 3. THE MEDICATION'S ROUTE, DOSAGE FORM, DOSAGE, AND ADMINISTRATION SCHEDULE (INCLUDING DURATION OF THERAPY)
- 4. DIRECTIONS FOR PREPARING AND USING OR ADMINISTERING THE MEDICATION
- 5. ACTION TO BE TAKEN IN CASE OF A MISSED DOSE
- 6. PRECAUTIONS TO BE OBSERVED DURING THE MEDICATION'S USE

CONTENT OF PATIENT COUNSELING: *ASHP GUIDELINES*

- 7. ADVERSE EFFECTS AND ACTIONS TO PREVENT OR MINIMIZE THEIR OCCURRENCE, INCLUDING THE NEED TO NOTIFY THE PRESCRIBER, OR PHARMACIST
- 8. TECHNIQUES FOR SELF-MONITORING OF THE PHARMACOTHERAPY
- 9. POTENTIAL DRUG–DRUG, DRUG–FOOD, AND DRUG–DISEASE INTERACTIONS OR CONTRAINDICATIONS
- 10. PROPER STORAGE AND DISPOSAL(OF CONTAMINATED OR DISCONTINUED) MEDICATIONS
- 11. ANY INFORMATION UNIQUE TO AN INDIVIDUAL PATIENT

BOOKLET EDUCATION



PEDIATRIC SURVIVORSHIP

- ADVANCES IN THE TREATMENT AND SUPPORTIVE MANAGEMENT RESULTED IN INCREASED
 OVERALL SURVIVAL OF CHILDREN TO APPROXIMATELY 80-85%¹
- 2/3 OF ADULT SURVIVOR OF PEDIATRIC CANCER WILL SUFFER FROM LONG TERM HEALTH CONDITIONS AND TOXICITIES

1.Bhatia S, Armenian SH, Armstrong GT, et al. J Clin Oncol. 2015;33(27):3055–3064.

PEDIATRIC SURVIVORSHIP

LATE COMPLICATIONS OF CANCER AND CANCER TREATMENT

- NEUROCOGNITIVE DEFECTS
- PERIPHERAL SENSORY NEUROPATHY
- ΟΤΟΤΟΧΙCΙΤΥ
- GONADAL DYSFUNCTION
- CARDIOVASCULAR COMPLICATION
- **RENAL TOXICITY**
- GROWTH HORMONE DEFICIENCY
- 2ND MALIGNANCY

CONCLUSION

- THE KNOWLEDGE AND SKILLS OF ONCOLOGY PHARMACIST SUPPORT A WIDE VARIETY OF FUNCTIONS IN ALL ASPECTS OF PATIENT CARE
- THE ONCOLOGY PHARMACIST IS OFTEN ONE OF THE FEW TEAM MEMBERS THAT FULLY UNDERSTANDS THE SAFETY, EFFICACY, PHARMACOLOGIC AND FINANCIAL COMPONENT OF PATIENT CARE IN INDIVIDUALS WITH CANCER
- THE CHANGING LANDSCAPE OF HEALTH CARE AND EVOLVING APPROACH TO CANCER CARE (EG. ORAL THERAPIES, TARGETED THERAPIES, PERSONALIZED MEDICINE) WILL EMPHASIZE THE NEED FOR THE ONCOLOGY HEALTH CARE TEAM TO INCLUDE AN ONCOLOGY PHARMACIST



THANK YOU FOR YOUR ATTENTION