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Drug interactions (7)). Determinations of whole blood clotting and bleeding time monitoring of warfarin sodium therapy.

The Standard Book and on the Standard Book and the Standard Book a

Warfarin codium may increase the acturate partial thromogalactic time (aPTT) sect, even in the absence of heparin. A reverse elevation (): 50 seconds) in aPTT with an INN in the desired range has been identified as an indication of increased risk of postagerative heronomous.

Other Asticoagulants
Consult the libeling of other anticoagulants for instructions on conversion to wordering oddurn.

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1.8 Newsork certain concombant drugs (see brug interactions (F)); and large duration of winters

Perform require monitoring of RNR in all treated patients. Those at high risk of biseding
may benefit from more frequent RNR monitoring, conful does adjustment to decide
NNR, and a shortest duration of therapy appropriate for the critical condition. However,
maintenance of RNR in the threatenance range does not eliminate them as of biseding. In your si The Therapeutic range does not element to the landing. Drugs, dietary changes, and other factors affect 196 levels actived with warfach sodium therape; Perform more frequent 198 months only when tarting or topping othe drugs, including botanicals, or when changing docupes of other drugs (see Drug interactions (7)).

interactions (7)).
Instruct patients about prevention measures to minimize risk of bleeding and to report signs and symptoms of bleeding [see Patient Counseling Information (17)].

been reported.

Careful circical evaluation is required to determine whether necrosis is caused by an underlying disease. Although various treatments have been attempted, no treatment for necrosor has been considered uniformly effective. Discontinue warfarin cookien therapy is Penetrials occurs. Consider attempts—during the continued anticopagation therapy is

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More frequent this monitoring should be performed when starting or stopping other drugs, including botanicals, or when changing dosages of other drugs, including drugs intended for short-term use (e.g., antibietics, antifungals, conticostersids) [see Bound Microsoft asarrings. Concut the labeling of all concurrently used drugs to obtain further information about interactions with warfarin codium or adverse reactions pertaining to bleeding.

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7.2 Drugs that increase Bleeding Risk Examples of drugs known to increase the risk of bleeding are presented in Table 3. Because bleeding risk it increased when these-drugs are used concentratly with warfain, closely monitor patients receiving any such drug with warfain.

Drug Class	Specific Drugs
	árgatroban, dabigatran, bivalnudin, desirudin, hepanin, lepinudin
ionsteroidal Anti- rifammatory Agents	celecoxib, diciofenac, diffunical, fenoprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, mefenamic acid, naproxen, oxaprozin, piroxicam, sulinda

3.3 Auditoria and Anthropais

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include your formatter planters administered workfor sodium housed sood any activity of vori that they were in thousement plant. The consequence of the planter of the control of the con Infants and chlaren receiving vitamin K-ruppiemented nutrition, including infant formulas, may be resistant to warfarin therapy, while human milk-fed infants may be sentition to warfarin therapy.

Patients 69 years or older appear to earbitist greater than expected MR response to the anticoappilater effects of warfars (see Chical Homeroscopy 22.28). Warfars socialism telescip and consideration also any exceptively patient with surjective Observer Caudion that anticolaryston of warfars socialism to eakery patients in any situation or with any ophytical condition where adoled risk of homorological prosents on any situation or with any ophytical condition where adoled risk of homorological prosents (concerning with present condition than other of warfars socialism in retainly patients (see bistage and administration of a condition of the co

Remarkant (s. p. 4, 2, 2).

Ref Renal Inspiratement.

Renal Clemence is considered to be a minor determinant of anticoagulant response to warfars. No docked-pulment is necessary for patients with renal impairment.

B. 7 Mayorit Experiment

Happic Repairment or potentials the response to warfarin through Impaired cyrithesis, or circumpture of control patients and docreased intensional or warfarin through impaired cyrithesis or circumpture of the control patients and docreased intensional or warfarin, the crudion when using warfars to allow in Stein patient.

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This treatment of excessive accompanion is based on the first firs rapid ne-articologistation is indicated, insparin may be prelimitable of establishments, Protocombic compiles concentrate (PCC), these frozano plannage a schalade fine-trap treatment may be considered if the requirement to review the infection of warfaint produced to the contract of the contract of the contract of the contract of the contract blood products (PCC and activated Factor VIII are also succeivate with an increased risk of thromosous. Prevention, these preparations should be used only in exceptional or life-threatening bleeding episodes secondary to warfant sodium overdosage.



Warfars station, 10°C is white crystallow resident it is very stable in water. Since share to color that described for one absolution countries which colors contributed to seal the color of the colo

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12.2 Pharmacokinetics
Warfarin codum is a racensic mixture of the A- and S-enantionners of warfarin. The S-enantionner enables 2 to 5 times more anticoagulars activity than the A-exantionner in humans, but generally has a more rapid classrace.

Absorption

Warfarin is eccentially completely absorbed after oral administration, with peak concentration generally attained within the first 4 hours.

Distribution

Wireful distribution (stop a relatively small apparent volume of distribution of about 0.16 L/kg. A distribution phase lasting 6 to 12 hours is distribution before one administration of an aqueous solution. Approximately 99% of the-drug is bound to

Design and the control of the contro

79, alor 11 alleris in Caucatario. Warfarin reduces the regiserantistic of vitamin K from vitamin K epoxide in the vitamin K cycle through inhibition of VMDR, a multiprotein enzyme complex. Certain single multiprotein programment in VMDRC1 gone (e.g., -1.616/co.1) towar been as occided with viriable wurtarin dose requirement. VMDRC1 and CMPDCV gone vurtams generally explain the legister propertion of it known viriability is wartarin dose requirements.

CIP2C9 and WORC1 genotype information, when available, can assist in selection of the initial does of worldon lives Doesage and Administration (2.31).

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itudy	N				Thrond	boembolism		i. Major Bleeding	
	Warfarin-Treated Patients	Control Patients	PT Radio	NR.	% Rick	Reduction	e-value	Warfarin-Treated Patients	Costn
NEASAK.	125	226	1.5-2	12		60	0.027	0.6	0
PAF	210	211	1.3-1.8			67	0.01	1.9	1.9
BAKTAF	212	208	12-15	15		86	<0.05	0.9	0.5
CAFA	197	191	1.3-1.6	2-2		45	0.25	2.7	0.5
POLAF	260	265	1.2-1.5	2.8		79	0.001	2.3	1.5

terminisgo strake and bandent kohema atlastic.

Trials in patients with both AF and mitral stances suggest a benefit from anticoaquistion with warfarin codium [see Dosage and Administration (2-3)].

A 2. Mechanical and Biopnosthetic Heart Values
In a prospective, randomised, open-basel positive-controlled study in 254 parkets with
microarcal prostate it have valued, the inhomostopic from transplant found to be
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(p-c0.05). The result	s of this study a	re precented in Table 5.	
Table SProsper	tive, Randomi	oed, Open-Label, Pucitiv s with Mechanical Prost	e-Controlled Clinical
actory or war	Will In Palient	Entinote Transact With	HELIL PRINT VANCES

In a prospective, open-label, clinical study comparing moderate (NR 2.65) versus. high intensity (NR II) wantarin threngies in 358 patients with michanical prosthetic heart valves, thromboembolism occurred with similar frequency in the two groups (4 and 3.7 events per 120 patient; years, respectively). May cheeking was more common in the

	oup. The results of						
Table 6Pro	spective, Open-I	abel Clinical : Prostheti	Study of Warfs C Heart Values	ein in Patie	nets with	Mechani	cal
Event	Moderate Wa	rfarin Therap	y INR 2.65 High	intensity		Therapy	1100

In a condomized trial in 210 parkets comparing two interactions of warfars transpay (RIR 2 to 2.5 vs. 1982 2.5 to 4) for a three month period following fiscus heart value registerers, three following fiscus or counted with character frequency in the face ground 1.2 disk, respectively. Right referenchings occurred in 6.6 for greater in the higher interacting Right group compared to zero in the lower interacting Right group.

of wascular death, are provided in Table 7.  Table 7WARIS - Endpoint Analysis of Separate Events						
Event	Warfarin (N+607)	Placebo (N=607)	RR (95% CI)	% Rick Reduction (a-value)		
Total Patient Years of follow-up	2018	1964				
Fotal Mortality	94 (4.7/000 py)	123 (6.3/100 py)	0.76 (0.60, 0.97)	04 (p+0.030		
/accubr Death	k2 (4.1/999 py)	105 (5.4100 py)	0.79 (0.60, 1.02)	22 (p+0.56)		
Recurrent Mi	k2 (6.1/000 py)	124 (6.4/100 py)	0.66 (0.51, 0.95)	M (p+0.00)		

WARTS in The Wasterin, Anglein, Ne-Infarction Study) was an open-lakel, randomized mudy of Skill plateers tougotable for acute reprocursion/rearction treated with wartson to a target RM 2.8 to 4.3, appen 500 reg per day, or authorito a target RM 2.8 to 2.5 composite of data, notated investments or Translatements translate and composite of data, notated investments or Translatements translate and of observation was approximately 4 years. The results for WARFS 8 are provided in the Table 8.

Event	Aspirin (N=1206)	Warfaris (N=1216) As No. of Events	pirin plus Warfarin (N+12	00)Rate Ratio (95% CI	p-value
Major Electings		22	28	3.39 (ND) 4.00 (ND)	ND ND
Minor lifeedings	29	109	133	3.21* (ND) 2.55* (ND)	ND ND
composite Endpoints*	241	203	191	0.91 (0.69-0.95)*	0.02
Reinfarction	117	90	69	0.56 (0.41-0.78)*	0.000
hromboembalk Strake	22	17	17	0.52 (0.29-0.99)	0.03

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15 REFERENCES

• CISHA Hazardous Drugs, CISHA.

http://www.osha.gov/SLTC/hazardousdrugs/index.html.

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This Redication founds summarized the most important information about warfarin 
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ask your healthcase provider or pharmacist for information about warfarin codium that 
it written for health profescionals. 
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