Non-calcium-based Phosphate Binders

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Objects

- Introduction
- Epidemiology (DOPPS)
- Non-Ca-based Phosphate Binders
- Rationale for class selection
- The Ph binder equivalent dose
- Take-home Message

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State-of-the-Art Management of Hyperphosphatemia in Patients With CKD: An NKF-KDOQI Controversies Perspective

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Question

- A 2017 online poll performed by the NKF-KDOQI asked the question "Should patients with CKD stage 3–5 (non-dialysis) & hyperphosphatemia receive noncalcium containing binders **only**?"

  1. **Yes**
  2. **No**

Julia J. AJKD. 2021

Introduction

- Among **979** respondents, only **46%** said “Yes,” indicating substantial **uncertainty** within the clinical community on whether non-calcium-based ph binders should be preferred in patients with CKD.

Julia J. AJKD. 2021

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2. Choose a category:

( ) Demographics ( ) Diabetes/Cardiovascular ( ) Anemia ( ) Potassium ( ) Dialysis Prescription and Dose

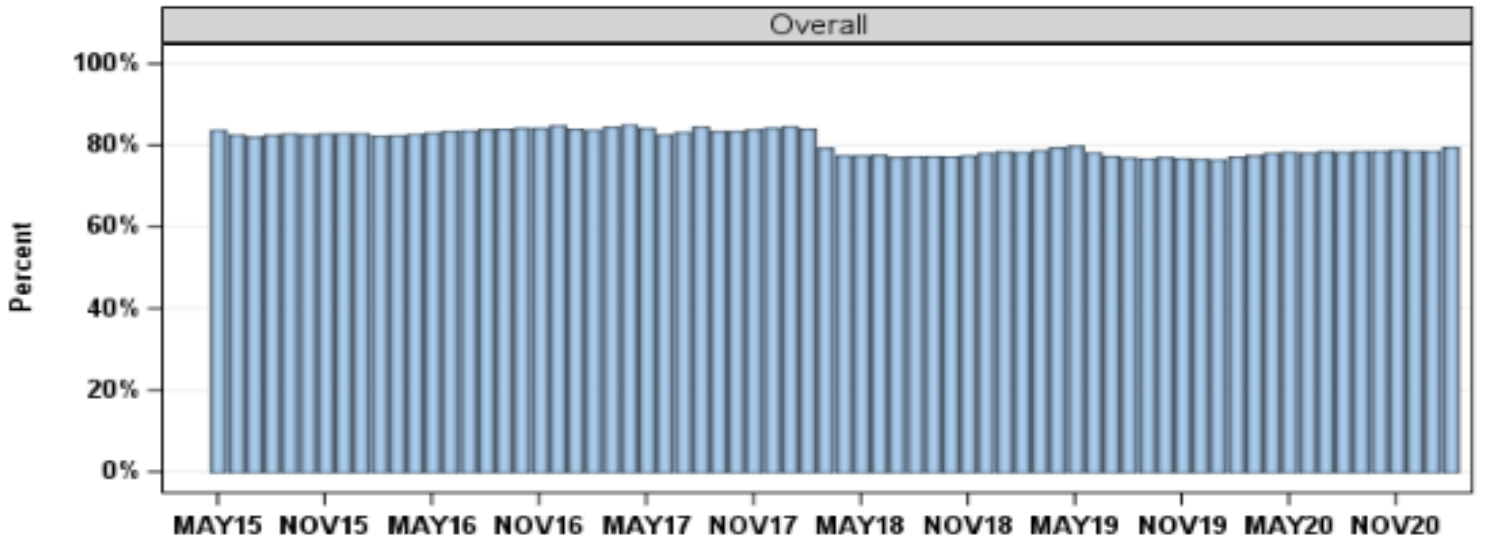
(•) Mineral and Bone Disorder ( ) Nutrition ( ) Vascular Access

3. Browse graphics:

- IV vitamin D type
- Use with calcimimetics
- Weekly IV vitamin D analog dose received
- Oral vitamin D analog use
- Vitamin D analog use
- Calcimimetics use
- Serum calcium (most recent)
- Serum calcium (3 month average)
- Serum phosphorus (most recent)
- Serum phosphorus (3 month average)
- Phosphate binder use
  - Use in last 1 month
    - National sample
    - Hospital-based/Free-standing
    - Race (Black/non-Black)

Phosphate binder use, last 1 month

National sample



Values for each month reflect prescription at end of study month (2010, 2011) or anytime during study month (2012+)

DOPPS PRACTICE MONITOR - HEMODIALYSIS

HD | United States | to DOPPS.org

Reporting contemporary trends in U.S. hemodialysis practice

Last Data Update: May 2021 (data through February 2021)

Featured Data | **Browse All Data** | **News & Publications** | **About DPM-HD**

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Featured Measure	National Sample	Key Messages	Related Slides
Dialysis Dose (Kt/V)			
Hemoglobin			
Serum Calcium			
Serum Phosphorus			
Serum PTH			
Serum Potassium			
IV Epoetin Dose (Received)			
IV Iron Use			
IV Vitamin D Use			
Calcimimetic Use			

(Mouse-over icon to view, Click icon to browse)

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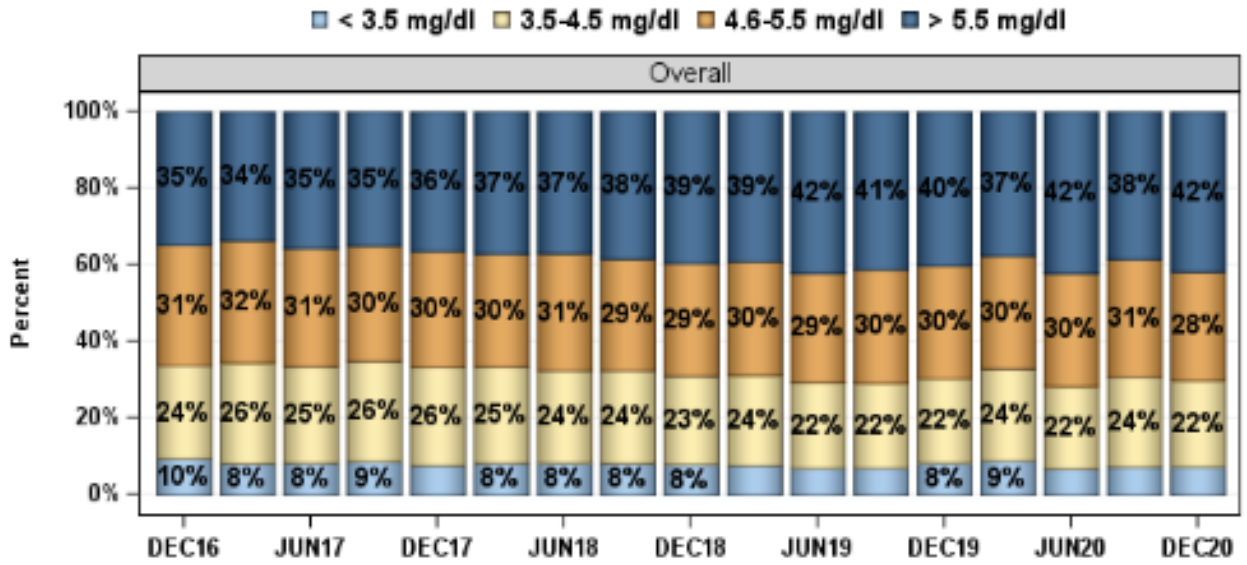
Serum phosphorus (most recent)

National sample



Most recent (single) monthly pre-dialysis value

Facility sample transitioned from DOPPS 4 to 5 in Jan-Apr 2012 (see "Study Sample and Methods").

Facility sample transitioned from DOPPS 5 to 6 in Mar-Jul 2015 (see "Study Sample and Methods").

Facility sample transitioned from DOPPS 6 to 7 in Feb-May 2018 (see "Study Sample and Methods").

Source: US-DOPPS Practice Monitor, May 2021; http://www.dopps.org/DPM

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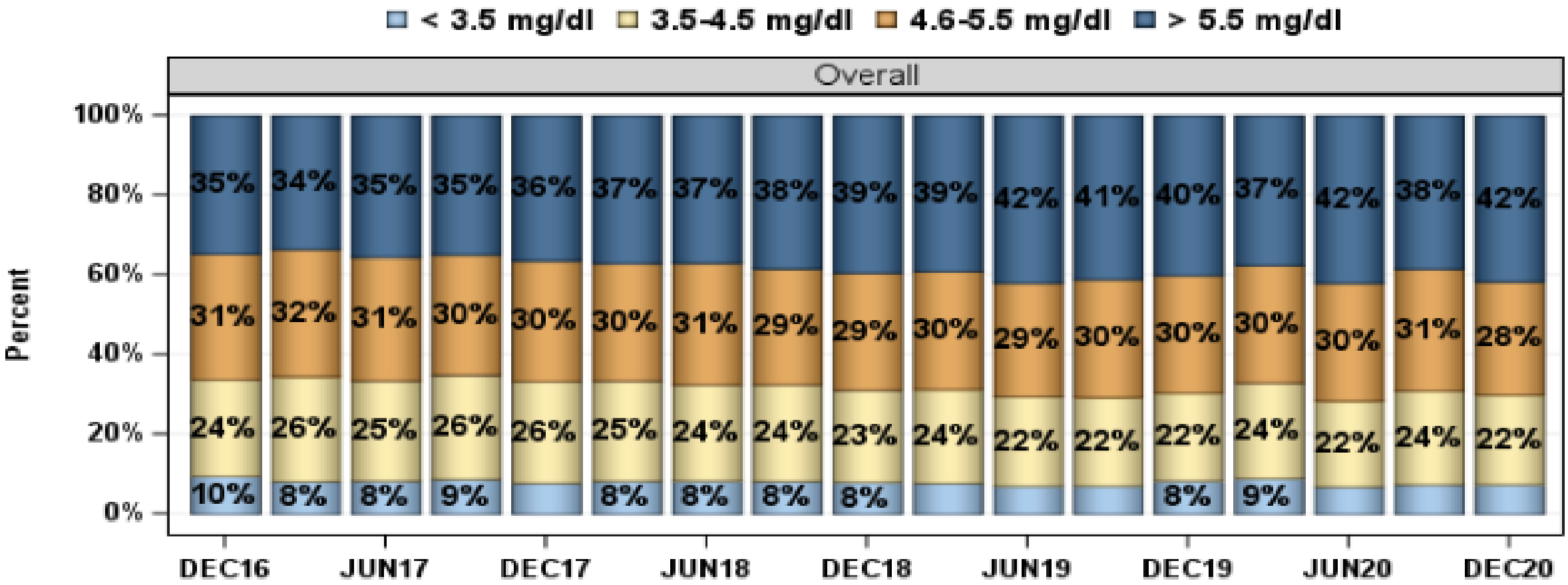
Serum phosphorus (most recent)

National sample



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3. Browse graphics:

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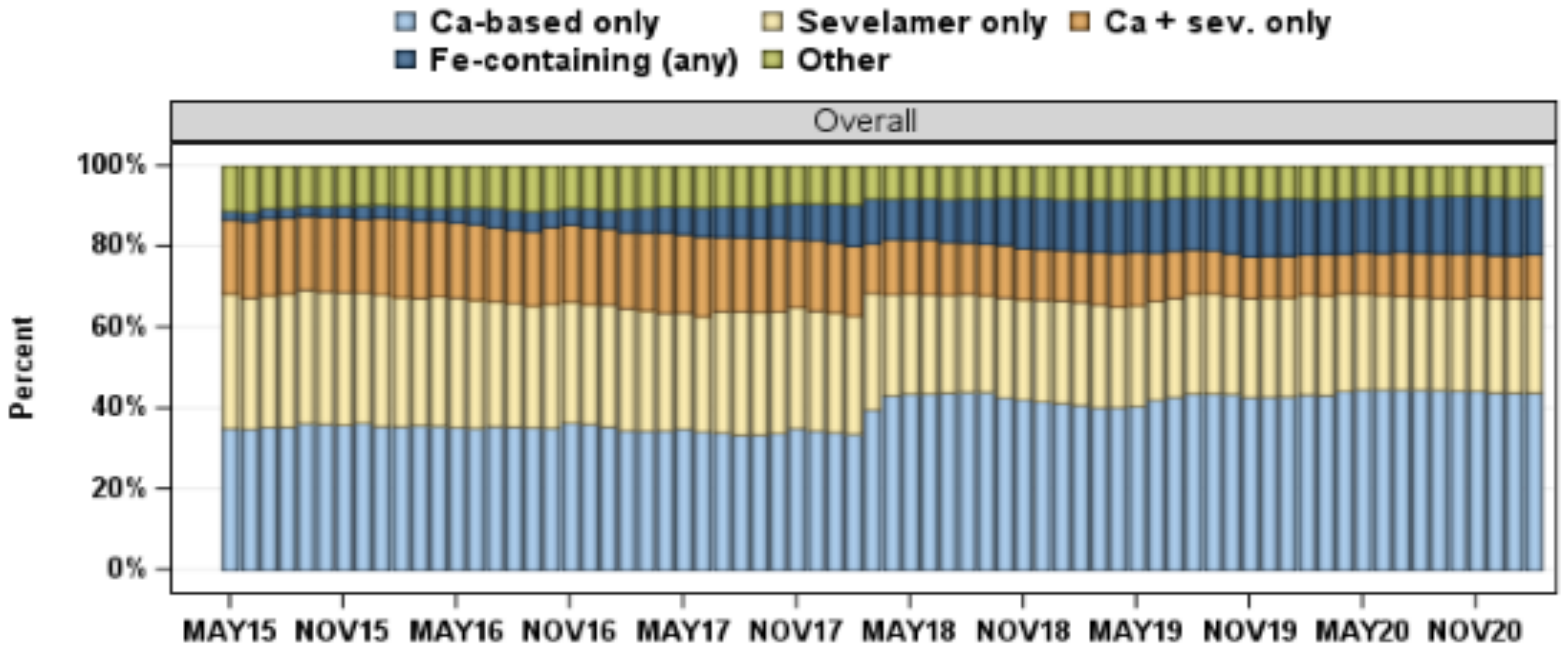
  - IV vitamin D analog use
  - Weekly IV vitamin D analog dose received
  - Oral vitamin D analog use
  - Vitamin D analog use
  - Calcimimetics use
  - Serum calcium (most recent)
  - Serum calcium (3 month average)
  - Serum phosphorus (most recent)
  - Serum phosphorus (3 month average)
  - Phosphate binder use
    - Use in last 1 month
    - Use in last 3 months
    - Phosphate binder type
      - National sample
      - Hospital-based/Free-standing
      - Race (Black/non-Black)
      - Incident (<90d)/prevalent (90+d)
    - Al- or Mg-containing use in last 3 months
    - Fe-containing use in last 3 months

Phosphate binder use, by type

National sample



Values for each month reflect prescription among patients prescribed a phosphate binder
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Facility sample transitioned from DOPPS 5 to 6 in Mar-Jul 2015 (see "Study Sample and Methods").
Facility sample transitioned from DOPPS 6 to 7 in Feb-May 2018 (see "Study Sample and Methods").
Source: US-DOPPS Practice Monitor, May 2021; http://www.dopps.org/DPM

Sample sizes and statistics for figure above - Understanding the DPM Figures - Share

Phosphate binder use, by type

			Ca-based only		Sevelamer only		Ca + sev. only		Fe-containing (any)		Other	
		Total N	N	Weighted %	N	Weighted %	N	Weighted %	N	Weighted %	N	Weighted %
National sample	Month											
Overall	MAY15	8,177	2,739	35.1%	2,856	33.4%	1,015	18.3%	139	2.1%	1,428	11.1%
	JUN15	8,507	2,868	35.0%	2,945	32.4%	1,043	19.0%	170	2.3%	1,481	11.4%
	JUL15	8,930	2,995	35.4%	3,118	32.6%	1,112	19.2%	189	2.4%	1,516	10.3%
	AUG15	8,937	3,010	35.5%	3,137	33.1%	1,116	18.8%	194	2.4%	1,480	10.2%
	SEP15	8,938	3,033	36.3%	3,136	33.1%	1,109	18.4%	204	2.4%	1,456	9.8%
	OCT15	8,974	3,028	36.2%	3,153	32.8%	1,118	18.6%	205	2.5%	1,470	9.9%
	NOV15	9,112	3,048	35.9%	3,183	32.9%	1,165	18.7%	222	2.7%	1,494	9.8%
	DEC15	9,038	3,043	36.4%	3,133	32.3%	1,142	18.3%	251	3.3%	1,469	9.6%
	JAN16	9,033	3,016	35.6%	3,135	32.6%	1,179	19.1%	255	3.1%	1,448	9.5%
	FEB16	9,092	3,049	35.6%	3,100	32.0%	1,195	19.5%	262	3.2%	1,486	9.8%
	MAR16	9,281	3,143	35.9%	3,122	31.5%	1,255	19.2%	272	3.4%	1,489	10.1%
	APR16	9,275	3,118	35.7%	3,107	31.9%	1,255	18.8%	275	3.4%	1,520	10.2%
	MAY16	9,292	3,165	35.4%	3,066	32.0%	1,249	18.6%	300	3.9%	1,512	10.1%
	JUN16	9,305	3,186	35.2%	3,032	31.7%	1,271	18.7%	315	4.3%	1,501	10.1%
	JUL16	9,268	3,205	35.6%	2,994	31.0%	1,229	18.3%	326	4.9%	1,514	10.2%
	AUG16	9,169	3,165	35.5%	2,947	30.6%	1,208	18.2%	341	5.0%	1,508	10.7%
	SEP16	9,082	3,102	35.4%	2,908	30.1%	1,229	18.4%	357	5.1%	1,486	11.1%
	OCT16	9,040	3,104	35.3%	2,857	30.7%	1,254	18.9%	338	4.3%	1,487	10.8%
	NOV16	9,112	3,177	36.4%	2,829	30.1%	1,272	19.0%	350	4.3%	1,484	10.2%
	DEC16	9,006	3,138	36.2%	2,809	29.7%	1,232	19.0%	358	4.7%	1,469	10.4%
	JAN17	8,921	3,109	35.5%	2,774	30.2%	1,226	19.0%	362	4.7%	1,450	10.7%
	FEB17	8,834	3,049	34.6%	2,710	30.2%	1,233	18.9%	401	5.8%	1,441	10.5%

Phosphate binder use, by type

			Ca-based only		Sevelamer only		Ca + sev. only		Fe-containing (any)		Other	
		Total N	N	Weighted %	N	Weighted %	N	Weighted %	N	Weighted %	N	Weighted %
National sample	Month											
	APR19	9,369	3,485	40.3%	2,357	24.8%	1,103	13.4%	954	13.2%	1,470	8.2%
	MAY19	9,314	3,450	40.6%	2,351	24.9%	1,075	13.3%	948	13.2%	1,490	8.1%
	JUN19	9,524	3,588	42.1%	2,429	24.5%	1,047	11.9%	961	13.2%	1,499	8.3%
	JUL19	9,824	3,740	42.9%	2,517	24.4%	1,099	11.7%	964	13.2%	1,504	7.8%
	AUG19	9,899	3,787	43.7%	2,538	24.8%	1,101	10.9%	971	12.9%	1,502	7.6%
	SEP19	10,324	3,896	43.7%	2,704	24.9%	1,168	10.6%	1,012	13.2%	1,544	7.7%
	OCT19	10,155	3,811	43.6%	2,608	24.3%	1,170	10.5%	1,048	13.9%	1,518	7.7%
	NOV19	10,010	3,748	42.8%	2,539	24.5%	1,140	10.3%	1,060	14.7%	1,523	7.7%
	DEC19	9,966	3,717	42.9%	2,535	24.6%	1,134	10.2%	1,047	14.1%	1,533	8.2%
	JAN20	9,946	3,684	43.0%	2,531	24.5%	1,135	10.4%	1,082	14.3%	1,514	7.9%
	FEB20	9,877	3,694	43.5%	2,504	24.7%	1,109	9.9%	1,068	13.9%	1,502	8.0%
	MAR20	10,079	3,783	43.3%	2,569	24.7%	1,126	10.2%	1,068	13.7%	1,533	8.1%
	APR20	9,967	3,768	44.3%	2,534	24.3%	1,076	9.7%	1,077	13.8%	1,512	8.0%
	MAY20	9,886	3,743	44.7%	2,500	23.9%	1,088	10.2%	1,066	13.6%	1,489	7.7%
	JUN20	9,795	3,701	44.7%	2,464	23.5%	1,081	10.3%	1,076	13.9%	1,473	7.6%
	JUL20	9,848	3,692	44.7%	2,518	23.1%	1,104	11.0%	1,069	13.8%	1,465	7.4%
	AUG20	9,798	3,672	44.6%	2,521	22.9%	1,094	10.9%	1,065	13.9%	1,446	7.6%
	SEP20	9,810	3,668	44.6%	2,527	22.8%	1,090	11.1%	1,069	14.2%	1,456	7.4%
	OCT20	9,687	3,578	44.3%	2,511	23.0%	1,071	11.1%	1,073	14.3%	1,454	7.3%
	NOV20	9,559	3,499	44.3%	2,493	23.4%	1,042	10.7%	1,082	14.3%	1,443	7.3%
	DEC20	9,441	3,450	43.9%	2,462	23.5%	1,020	10.6%	1,091	14.6%	1,418	7.4%
	JAN21	9,432	3,453	43.9%	2,471	23.5%	1,012	10.6%	1,080	14.4%	1,416	7.6%
	FEB21	8,565	3,173	43.9%	2,229	23.4%	937	10.9%	983	14.3%	1,243	7.5%

Values for each month reflect prescription among patients prescribed a phosphate binder
Facility sample transitioned from DOPPS 4 to 5 in Jan-Apr 2012 (see "Study Sample and Methods").
Facility sample transitioned from DOPPS 5 to 6 in Mar-Jul 2015 (see "Study Sample and Methods").
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Source: US-DOPPS Practice Monitor, May 2021; http://www.dopps.org/DPM

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Germany

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Reporting contemporary trends in German dialysis practice

Last Data Update: June 2016 (data through March 2015)

1. Choose a category:

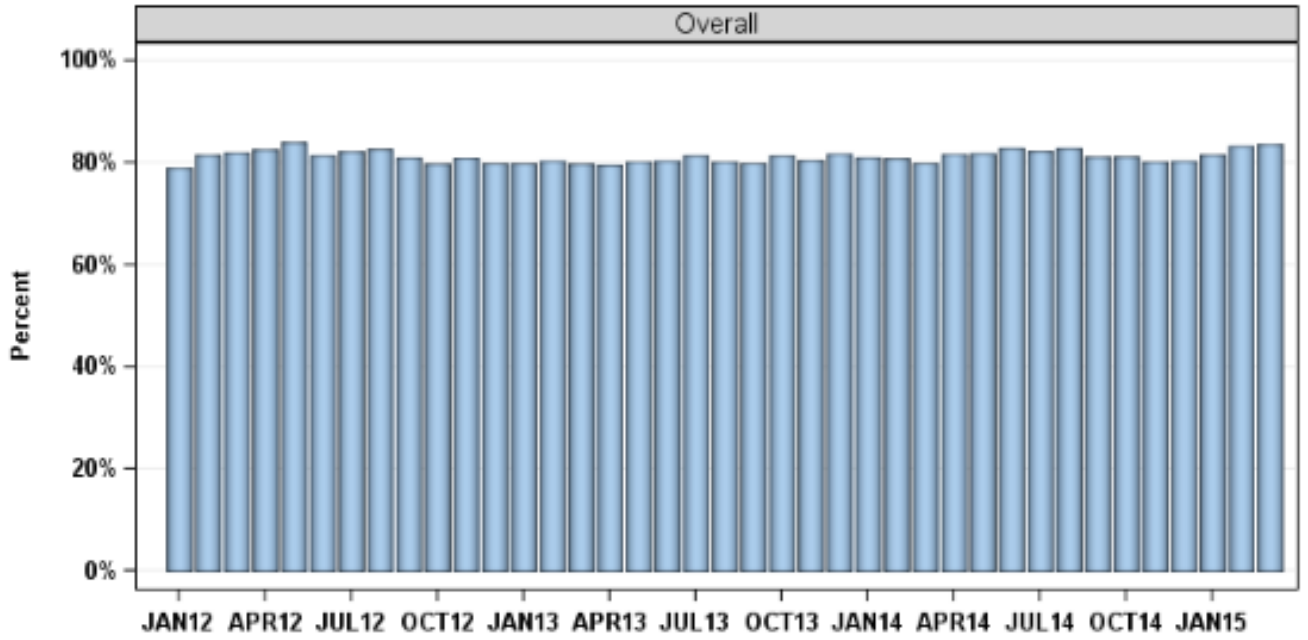
○ Demographics ○ Comorbidities ○ Anemia ○ Dialysis Prescription and Dose ◉ Mineral and Bone Disorder

○ Nutrition ○ Vascular Access

- Mineral and Bone Disorder
  - Serum calcium (most recent)
    - Albumin-corrected, categories
    - Albumin-corrected, continuous
    - Total, categories
    - Total, continuous
  - Serum calcium (3 month average)
  - Serum phosphorus (most recent)
  - Serum phosphorus (3 month average)
  - Serum PTH (most recent)
  - Serum PTH (3 month average)
  - Phosphate binder use
    - Use in last 1 month
    - Use in last 3 months
    - Phosphate binder type
    - Al- or Mg-containing use in last 3 months
    - La-containing use in last 3 months
  - Cinacalcet use
  - Vitamin D analog use
  - IV vitamin D analog use

Phosphate binder use, last 1 month

National sample



Values for each month reflect any prescription during prior month

Facility sample transitioned from DOPPS 4 to 5 in Jan-Apr 2012 (see "Study Sample and Methods").

Facility sample transitioned from DOPPS 5 to 6 in Mar-Jul 2015 (see "Study Sample and Methods").

Source: Germany-DOPPS Practice Monitor, June 2016

Phosphate binder use, last 1 month

		N Ptnts	Total N	Wgtd %
National sample	Month			
Overall	JAN12	245	309	79.0%
	FEB12	387	473	81.5%
	MAR12	391	482	82.0%
	APR12	420	521	82.6%
	MAY12	413	509	84.0%
	JUN12	427	535	81.4%
	JUL12	433	541	82.2%
	AUG12	437	543	82.6%
	SEP12	416	529	81.0%
	OCT12	407	532	79.7%
	NOV12	418	534	80.9%
	DEC12	419	542	79.8%
	JAN13	441	568	79.8%
	FEB13	440	564	80.3%
	MAR13	443	569	79.8%
	APR13	445	575	79.5%
	MAY13	443	572	80.2%
	JUN13	452	582	80.4%
	JUL13	455	574	81.4%
	AUG13	450	580	80.2%
	SEP13	464	596	79.9%
	OCT13	467	591	81.3%
	NOV13	460	591	80.5%
	DEC13	468	595	81.7%
	JAN14	463	592	81.0%
	FEB14	465	589	80.8%
	MAR14	461	588	79.9%
	APR14	474	597	81.7%
	MAY14	470	587	81.8%
	JUN14	482	592	82.8%
	JUL14	481	593	82.3%
	AUG14	486	599	82.8%
	SEP14	475	596	81.1%
	OCT14	479	596	81.2%
	NOV14	476	601	80.2%
	DEC14	471	595	80.3%
	JAN15	457	564	81.5%
	FEB15	461	555	83.2%
	MAR15	451	544	83.6%

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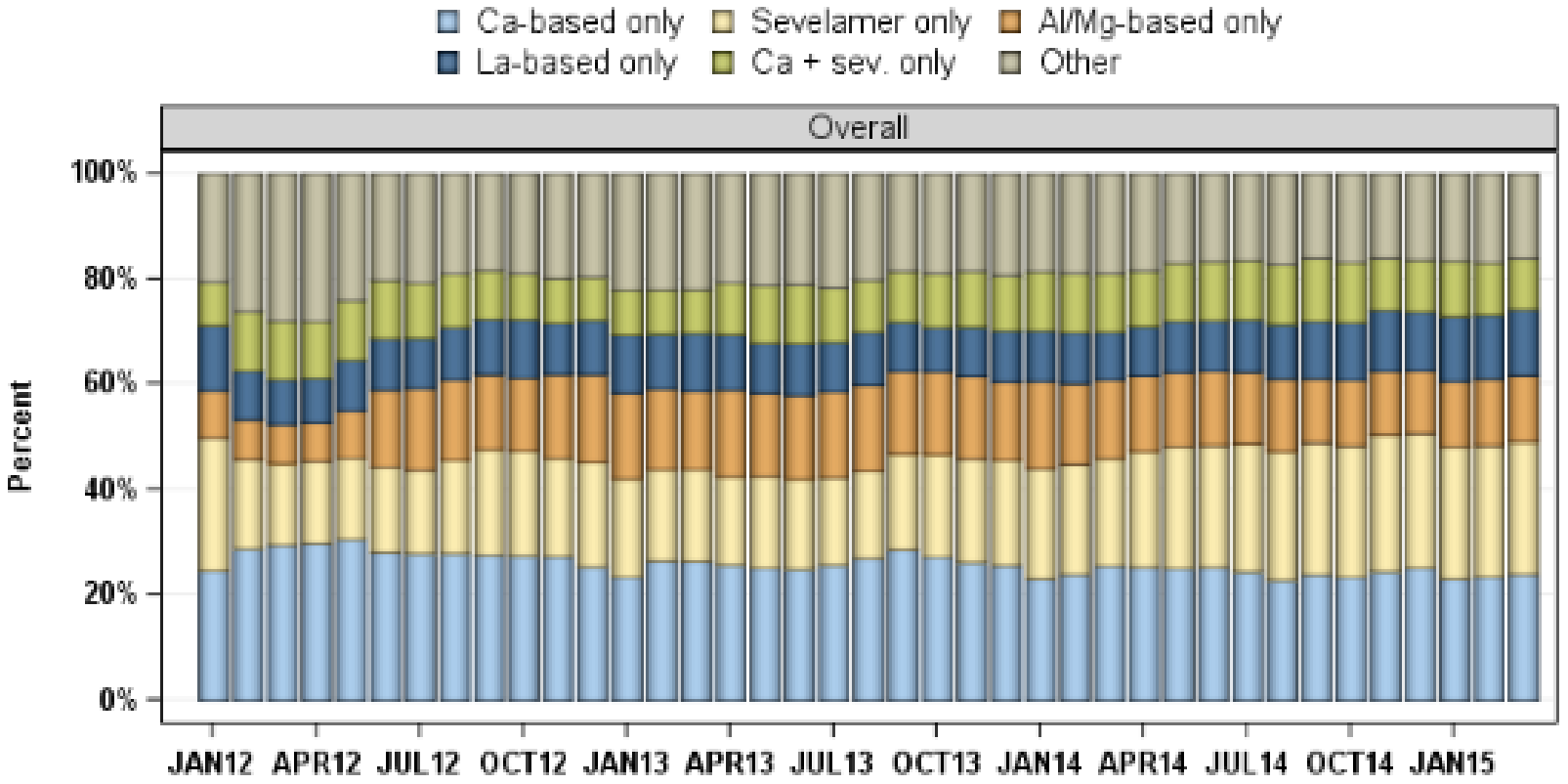
Phosphate binder use, by type

National sample



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Phosphate binder use, by type

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		Total N	N Ptnts	Pct	N Ptnts	Pct	N Ptnts	Pct	N Ptnts	Pct	N Ptnts	Pct	N Ptnts	Pct
National sample	Month													
Overall	JAN12	245	64	24.5%	54	25.2%	24	9.0%	31	12.5%	19	8.3%	53	20.5%
	FEB12	387	111	28.7%	63	17.1%	35	7.4%	39	9.3%	39	11.4%	100	26.1%
	MAR12	391	116	29.5%	58	15.6%	35	7.3%	36	8.5%	41	11.1%	105	28.0%
	APR12	420	125	29.8%	69	15.7%	34	7.2%	38	8.5%	42	10.8%	112	28.1%
	MAY12	413	128	30.5%	71	15.6%	39	8.8%	41	9.7%	42	11.4%	92	24.0%
	JUN12	427	125	28.1%	73	16.3%	57	14.5%	43	9.8%	43	11.1%	86	20.2%
	JUL12	433	126	27.9%	74	15.9%	59	15.5%	42	9.6%	42	10.4%	90	20.7%
	AUG12	437	125	27.9%	83	17.8%	62	15.2%	44	10.0%	39	10.1%	84	19.0%
	SEP12	416	120	27.6%	87	20.2%	54	14.2%	46	10.5%	34	9.3%	75	18.3%
	OCT12	407	115	27.4%	87	19.9%	52	13.9%	45	11.1%	31	8.7%	77	18.9%
	NOV12	418	117	27.3%	87	18.8%	59	15.9%	43	9.7%	31	8.6%	81	19.8%
	DEC12	419	110	25.3%	91	19.9%	62	16.7%	47	10.4%	29	8.2%	80	19.6%
	JAN13	441	108	23.3%	89	18.8%	64	16.2%	54	11.1%	31	8.6%	95	22.0%
	FEB13	440	119	26.4%	83	17.5%	62	15.3%	52	10.5%	30	8.4%	94	21.9%
	MAR13	443	118	26.3%	84	17.6%	63	14.7%	55	11.1%	31	8.3%	92	21.9%
	APR13	445	118	25.7%	82	16.9%	68	16.4%	52	10.5%	35	9.8%	90	20.7%
	MAY13	443	114	25.0%	83	17.6%	64	15.6%	45	9.5%	44	11.0%	93	21.2%
	JUN13	452	119	24.8%	82	17.2%	65	15.8%	48	9.8%	43	11.3%	95	21.0%
	JUL13	455	122	25.7%	81	16.7%	67	16.2%	46	9.4%	42	10.4%	97	21.6%
	AUG13	450	123	26.9%	79	16.6%	69	16.3%	47	10.1%	40	9.9%	92	20.1%
	SEP13	464	134	28.5%	89	18.4%	69	15.6%	45	9.4%	41	9.7%	86	18.4%
	OCT13	467	129	27.1%	93	19.7%	70	15.6%	42	8.5%	44	10.2%	89	18.9%
	NOV13	460	123	26.2%	92	19.8%	69	15.7%	43	9.3%	46	10.6%	87	18.4%
	DEC13	468	123	25.6%	95	20.1%	66	14.8%	46	9.8%	47	10.6%	91	19.2%
	JAN14	463	108	22.9%	101	21.1%	73	16.5%	45	9.7%	46	11.3%	90	18.5%
	FEB14	465	113	23.8%	102	21.1%	68	15.3%	45	9.7%	45	11.3%	92	18.8%
	MAR14	461	117	25.4%	100	20.6%	66	14.9%	43	9.1%	45	11.1%	90	18.9%
	APR14	474	121	25.2%	106	22.1%	68	14.3%	44	9.4%	44	10.6%	91	18.4%
	MAY14	470	117	25.0%	110	23.3%	64	14.0%	44	9.8%	49	11.1%	86	16.9%
	JUN14	482	119	25.2%	111	23.2%	68	14.1%	46	9.7%	51	11.2%	87	16.6%
	JUL14	481	117	24.4%	115	24.3%	66	13.6%	46	10.0%	51	11.3%	86	16.4%
	AUG14	486	112	22.7%	119	24.6%	68	13.8%	47	10.4%	52	11.3%	88	17.2%
	SEP14	475	118	23.8%	120	25.1%	57	12.2%	49	10.9%	51	12.1%	80	15.9%
	OCT14	479	116	23.3%	121	25.1%	59	12.4%	49	11.0%	50	11.4%	84	16.8%
	NOV14	476	120	24.4%	125	26.0%	58	12.1%	51	11.7%	45	9.9%	77	15.9%
	DEC14	471	122	25.0%	122	25.5%	58	12.0%	48	11.3%	44	9.9%	77	16.3%
	JAN15	457	104	23.0%	115	25.3%	58	12.3%	52	12.4%	46	10.6%	82	16.5%
	FEB15	461	108	23.3%	115	25.1%	60	12.7%	51	12.1%	42	9.9%	85	16.9%
	MAR15	451	111	23.9%	110	25.2%	59	12.6%	51	12.6%	41	9.7%	79	16.0%

Values for each month reflect prescription among patients prescribed a phosphate binder
Facility sample transitioned from DOPPS 4 to 5 in Jan-Apr 2012 (see "Study Sample and Methods").
Facility sample transitioned from DOPPS 5 to 6 in Mar-Jul 2015 (see "Study Sample and Methods").
Source: Germany-DOPPS Practice Monitor, June 2016

Overall evidence for ph binding therapy in CKD stages G3–5 ND

- Serum ph concentrations typically remain normal until late in CKD, with clinically important rates of hyperphosphatemia not evident until CKD **G4.**
- Nr levels of serum ph are maintained by activation of the regulatory hormones **PTH** & **FGF23**.
  - Both increase the FE of ph in the urine to promote excretion as GFR falls.
  - FGF23 also limits GI ph absorption by reducing levels of 1,25 OHvit D.
- In addition to known effects on bone, changes in many of these biochemical parameters are associated with risks of CVD & death.

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Overall evidence for ph binding therapy in CKD stages G3–5 ND

Patient-centered & clinical outcomes studies are needed before use of ph binders, of any type, can be recommended in patients with CKD G3–5 (non-dialysis) except to control symptomatic or severe hyperphosphatemia.

Julia J. AJKD. 2021

Overall evidence for ph binding therapy in kidney failure

- Hyperph may become severe in KF, resulting in symptoms & well-described clinical complications, such as **bone disease, calciphylaxis, & itching**.
- For this reason, use of binders to prevent clinically important hyperph is **justified**.
- In our view, intensive use of ph binders to specific targets aiming to prevent potential cardiovascular consequences requires evaluation in **trials**.

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Non-Ca-based Phosphate Binders

- Sevelamer Hydrochloride
- Sevelamer Carbonate
- Lanthanum Carbonate
- Sucroferric Oxyhydroxide
- Ferric Citrate
- Tenapanor

Sevelamer Hydrochloride

FDA approval: 1998

Sevelamer Hydrochloride

- **Mechanism of Action:**
  - Exchanges chloride for Ph
- **Potential Advantages:**
  - Ca free
  - Pleiotropic effects
  - May reduce vascular calcification
- **Potential Disadvantages**
  - Expensive
  - GI side effects
  - Metabolic acidosis
  - Limit fat soluble vitamin absorption
- **Dose Considerations:**
  - Tablet 800–1,600 mg 3 times/day
  - Maximum dose: 13 g/day
- **~ P Binder Equivalence:**
  - 0.6 for 800 mg tablet

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Sevelamer Hydrochloride: dose

Serum Ph	Renagel® 800 mg
> 5.5 and < 7.5 mg/dL	1 tablet 3 times daily with meals
≥ 7.5 and < 9.0 mg/dL	2 tablet 3 times daily with meals
≥ 9.0 mg/dL	3 tablet 3 times daily with meals

https://reference.medscape.com/drug/

Oral drugs interaction with Sevelamer

- Ciprofloxacin
  - Take at least 2 hs before or 6 hs after sevelamer
- Mycophenolate mofetil
  - Take at least 2 hs before Sevelamer
- May decrease GI absorption of antiarrhythmic, fat soluble vitamins, folic acid, & antiseizure medications; take medications 1 h before or 3 hs after sevelamer dose

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frontiers in Medicine

ORIGINAL RESEARCH
published: 25 November 2021
doi: 10.3389/fmed.2021.714205

IF: 5.091

Cruz END. Frontiers in Medicine. 2021

The Influence of Sevelamer Hydrochloride and Calcium Carbonate on Markers of Inflammation and Oxidative Stress in Hemodialysis at Six Months of Follow-Up

Elodia Nataly Díaz-De la Cruz[1], *José Ignacio Cerrillos-Gutiérrez*[2], *Andrés García-Sánchez*[1], *Carlos Gerardo Prado-Nevárez*[2], *Jorge Andrade-Sierra*[2], *Basilio Jalomo-Martínez*[2], *Adriana Banda-López*[2], *Enrique Rojas-Campos*[2] *and*

OPEN ACCESS

Calcium carbonate Mechanism of action

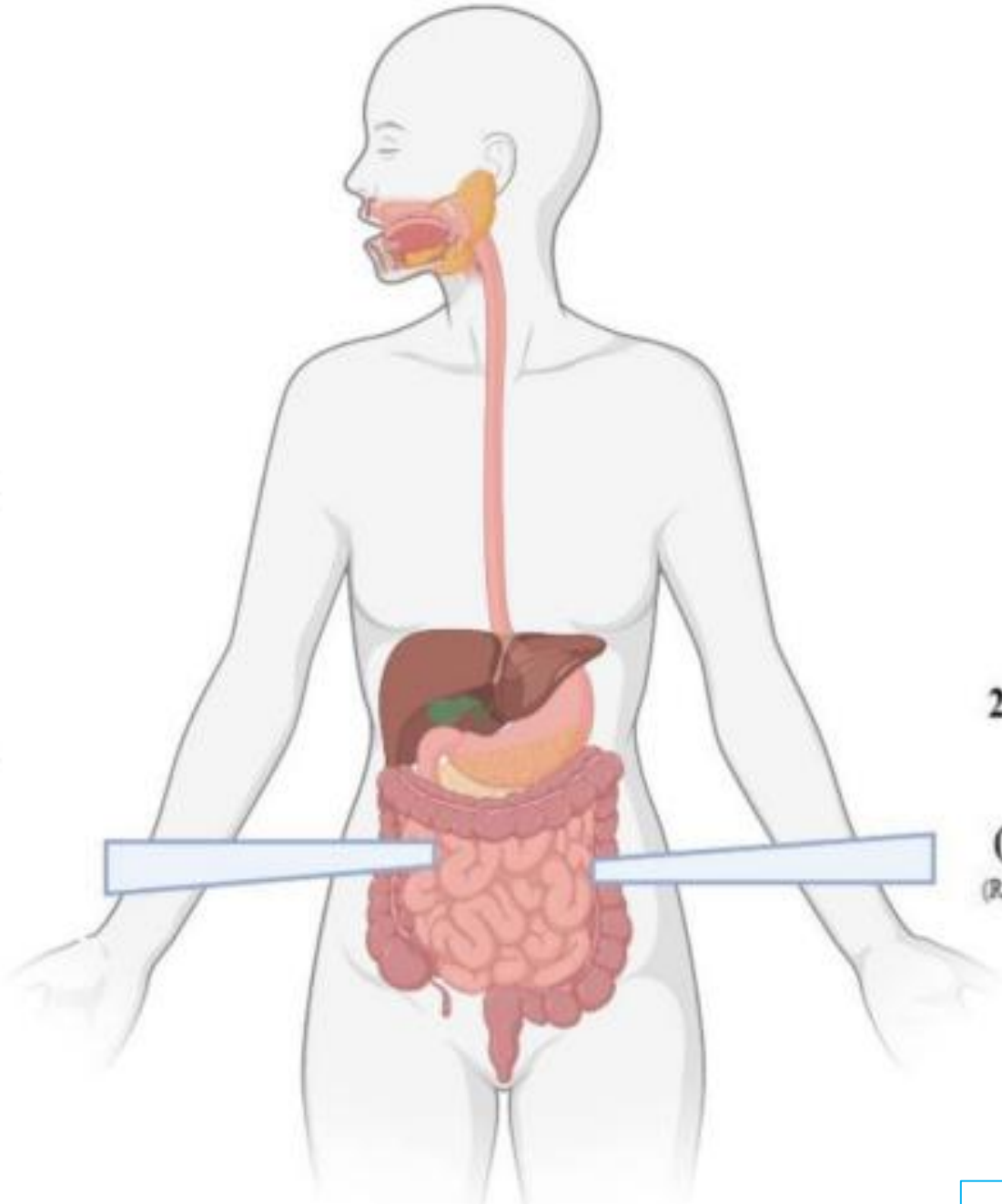
$3\ CaCO_3 + 2\ H_3PO_4 \longrightarrow$

Calcium carbonate

$Ca_3(PO_4)_2 + CO_2 + H_2O$

Calcium phosphate

Excreted in feces



Sevelamer hydrochloride Mechanism of action

$2\ (R\text{-}N^+H_3Cl^-) + HPO_4^{-2} \rightleftharpoons$

(Resin-chloride form)

Ion-exchange

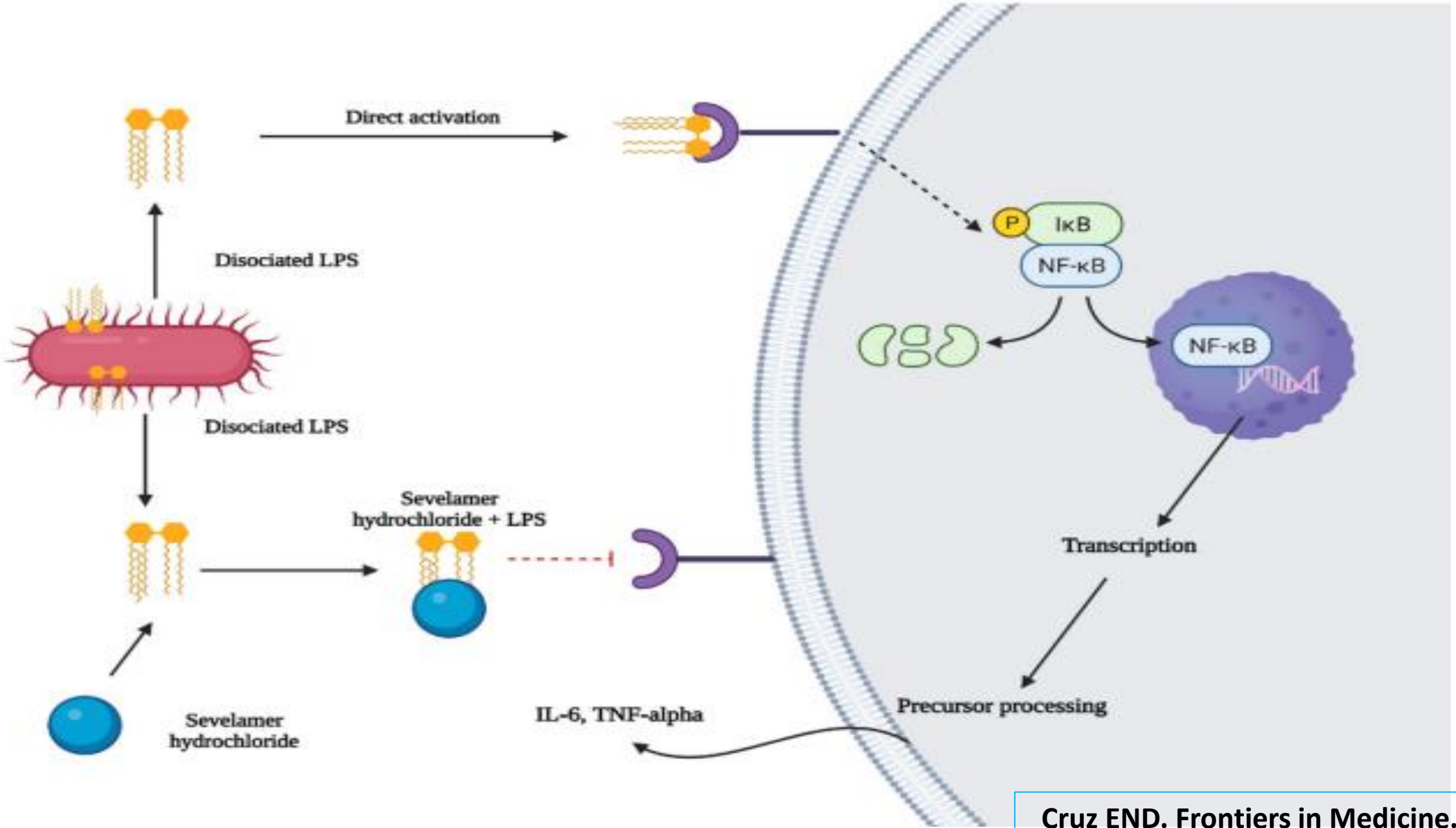
$(R\text{-}N^+H_3)_2HPO_4^{-2} + Cl^-$

(Resin-divalent phosphate form)

Excreted in feces

Cruz END. Frontiers in Medicine. 2021

Anti-inflammatory mechanism of sevelamer hydrochloride



Cruz END. Frontiers in Medicine. 2021

Conclusion

The management of hyperphosphatemia with Sevelamer hydrochloride appears to have obvious **anti-inflammatory** & **antioxidant benefits**.

Cruz END. Frontiers in Medicine. 2021

Sevelamer Hydrochloride in IRAN

نام دارو	داروسازی
تولامر Tavelamer	تسنیم (کربنات)
ریبامر Ribumer	امین (هیدروکلراید)
سولامر زهراوی Sevelamer Zahravi	زهراوی
رنالایو – رناهلت Renalive - Renahealth	سها (هیدروکلراید – کربنات)
سواژل– اکسیلامر Exilamer - Sevagel	اکسیر(هیدروکلراید – کربنات)
سولاوین Sevelavin	اوه سینا (هیدروکلراید)
ردوفو – رنوفا Redupho - Renofa	فاران شیمی (هیدروکلراید – کربنات)
سولوگر Seveloger	هوگر دارو دانش (کربنات)

Sevelamer Carbonate

FDA approval: 2007

Sevelamer Carbonate

- Mechanism of Action:
  - Exchanges carbonate for P
- Potential Advantages:
  - Ca free
  - Pleiotropic effects
  - No metabolic acidosis
  - May reduce vascular calcification
- Potential Disadvantages:
  - Expensive
  - GI side effects
  - Limit fat soluble vitamin absorption

- Forms: Tablet, Powder
- Dose Considerations:
  - 800–1,600 mg 3 times/day
  - Maximum dose: **14 g**/day
- **~ P Binder Equivalence:**
  - **0.6** for 800 mg tablet

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Lanthanum Carbonate

FDA approval: 2004

Lanthanum Carbonate (Fosrenol)

- Mechanism of Action:
  - Forms insoluble metal & P complexes
- Potential Advantages:
  - Ca free
- Potential Disadvantages:
  - Expensive
  - Unclear risk for metal accumulation
  - GI side effects
  - No long-term data

- Forms: Chewable tablet, Powder
- Dose Considerations:
  - 500–1,000 mg 3 times/day
- **~ P Binder Equivalence:**
  - **1.0** for 500 mg table

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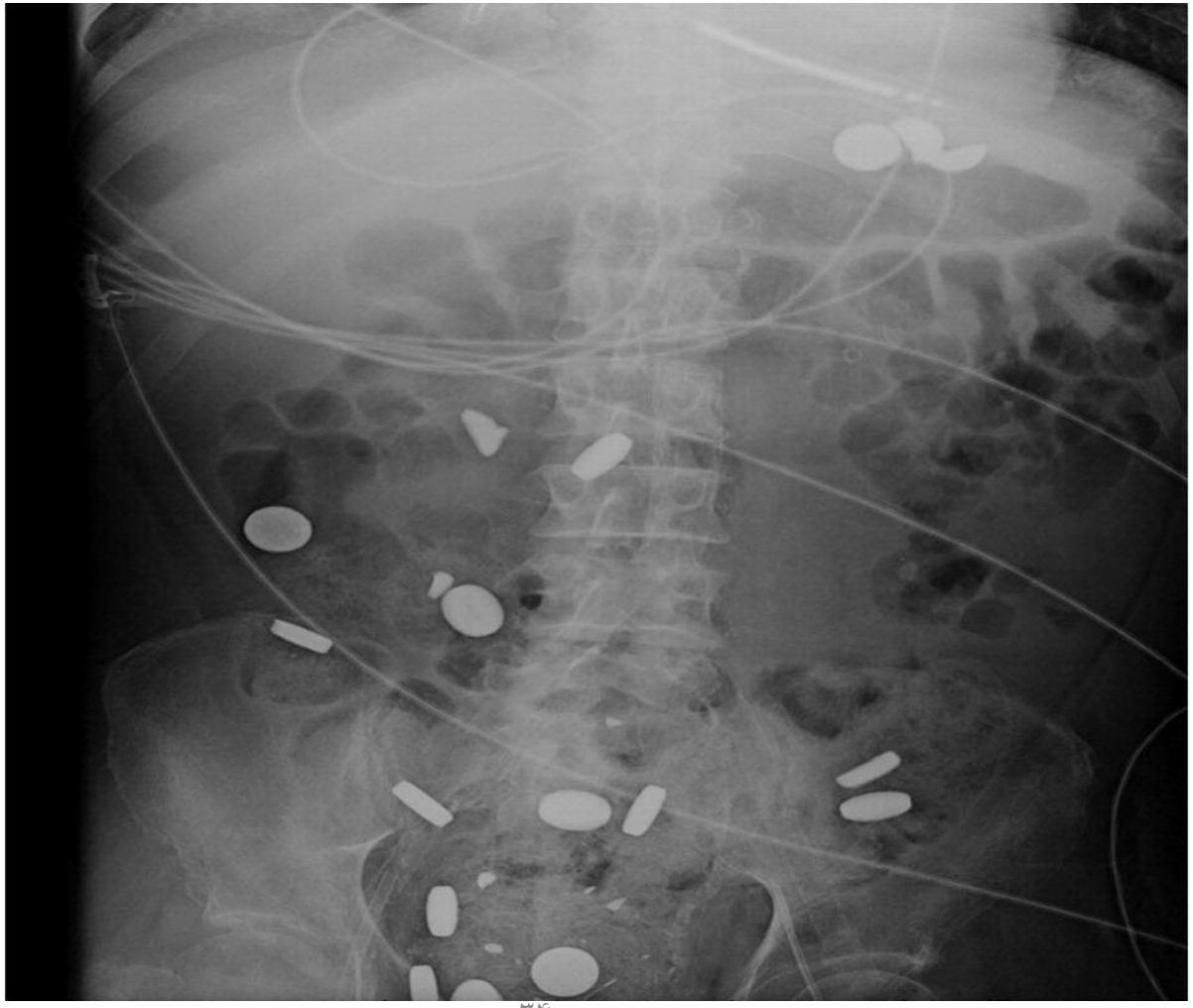
Lanthanum Carbonate (Fosrenol)

- Has **radio-opaque properties** & therefore may give the appearance typical of an imaging agent during abdominal X-ray procedures
- Chewable tablets should be **chewed completely** to reduce the risk of serious adverse GI events



Moazzam AA. AJKD.2013

Sucroferric Oxyhydroxide

FDA approval: 2013

Sucroferric Oxyhydroxide (Velphoro)

- Mechanism of Action:
  - Exchanges hydroxyl for P
- Potential Advantages:
  - Ca free
  - Lower pill burden
- Potential Disadvantages:
  - Expensive
  - GI side effects
  - Interferes with oral levothyroxine
  - Long-term side effects unknown
  - Unclear risk of iron accumulation

- Forms: Chewable tablet
- Dose Considerations:
  - 2.5 g 3 times/day
  - 500 mg iron per 2.5 g tab
  - Maximum dose: 6 tablets/day
- **~ P Binder Equivalence:**
  - **1.6** for 2.5g tablet

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Sucroferric Oxyhydroxide (Velphoro)

- Do not prescribe with oral **levothyroxine**
- Do not administer **alendronate** or **doxycycline** at the same time;
  - Must be given at least 1 hr before sucroferric oxyhydroxide
- The sucrose & starch components can be digested to glucose & fructose, & maltose & glucose, respectively; these compounds can be absorbed in the blood (1 tablet = **1.4 g of carbohydrates**)
- Median iron update in patients with CKD is **0.04%** on Day 21 (based on 2,000 mg/day of sucroferric oxyhydroxide/day)

https://reference.medscape.com/drug/

Ferric Citrate

FDA approval: 2014

Ferric Citrate (Auryxia)

- Mechanism of Action:
  - Forms insoluble Fe3+ & P complexes
- Potential Advantages:
  - Ca free
  - Raises iron stores & Hb
  - Decrease iron & ESA usage
- Potential Disadvantages:
  - Expensive
  - GI side effects
  - Long-term side effects unknown
  - Unclear risk of iron accumulation

- Forms: Tablet
- Dose Considerations:
  - 2 g 3 times/day
  - 210 mg ferric iron per 1 g tablet
  - Maximum dose: 12 tablets/day
- **~ P Binder Equivalence:**
  - **0.64** for 1g tablet

Julia J. AJKD. 2021

Ferric Citrate (Auryxia)

- May lead to excessive elevations in iron stores
- Assess iron parameters before initiating drug & monitor parameters while on therapy
- Patients receiving IV iron may require a reduced dose or D/C
- Do not chew or crush tablets because tablets may cause discoloration of mouth & teeth

https://reference.medscape.com/drug/

Drugs (2019) 79:957–968
https://doi.org/10.1007/s40265-019-01125-w

IF: 9.546

REVIEW ARTICLE

Mechanism of Action and Clinical Attributes of Auryxia® (Ferric Citrate)

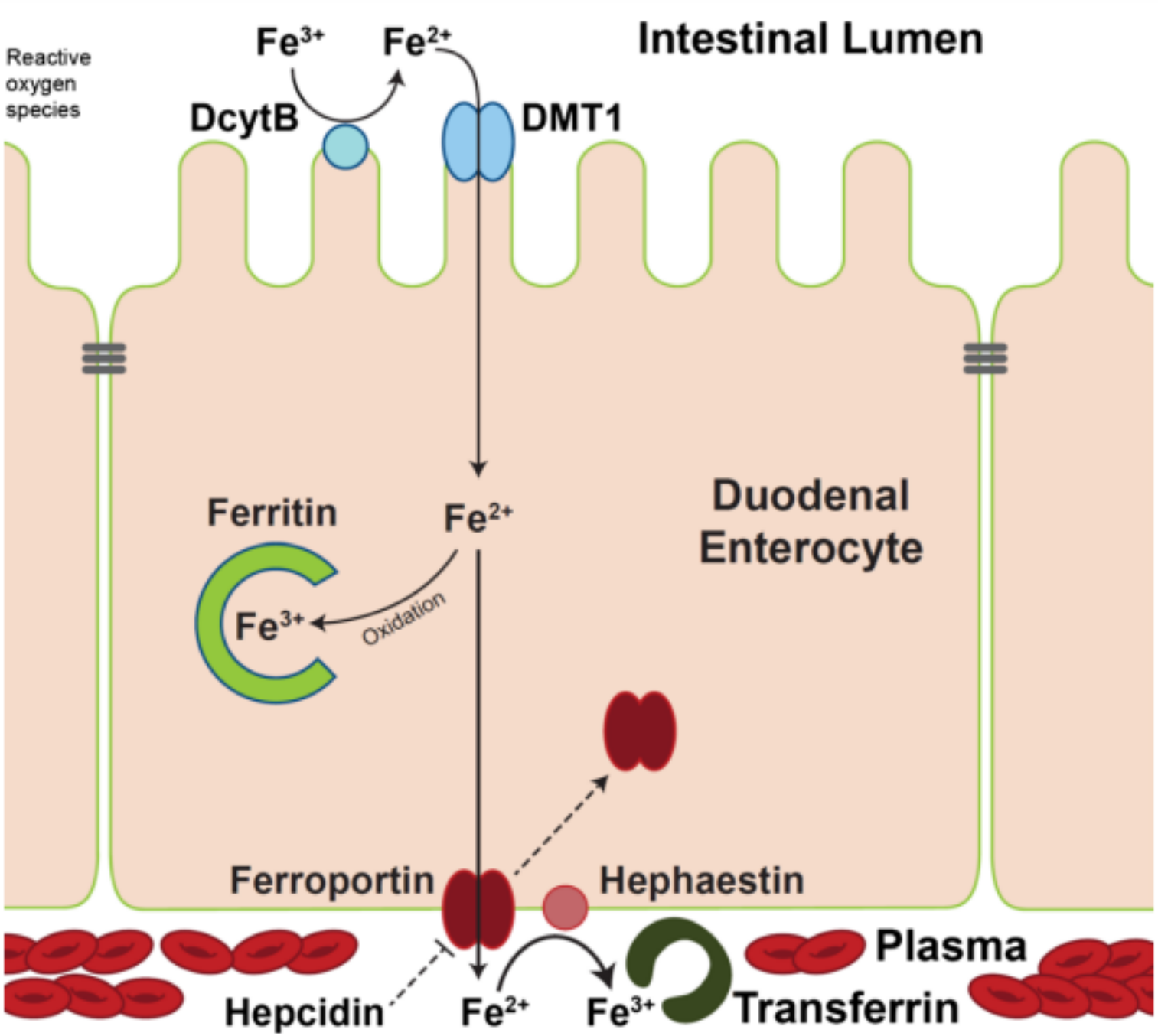
Tomas Ganz[1,3,4] · Avi Bino[2] · Isidro B. Salusky[1]

Published online: 27 May 2019

Abstract

Chronic kidney disease (CKD) is a major cause of morbidity and premature mortality and represents a significant global public health issue. Underlying this burden are the many complications of CKD, including mineral and bone disorders, anemia, and accelerated cardiovascular disease. Hyperphosphatemia and elevated levels of fibroblast growth factor 23 (FGF23) have been identified as key independent risk factors for the adverse cardiovascular outcomes that frequently occur in patients

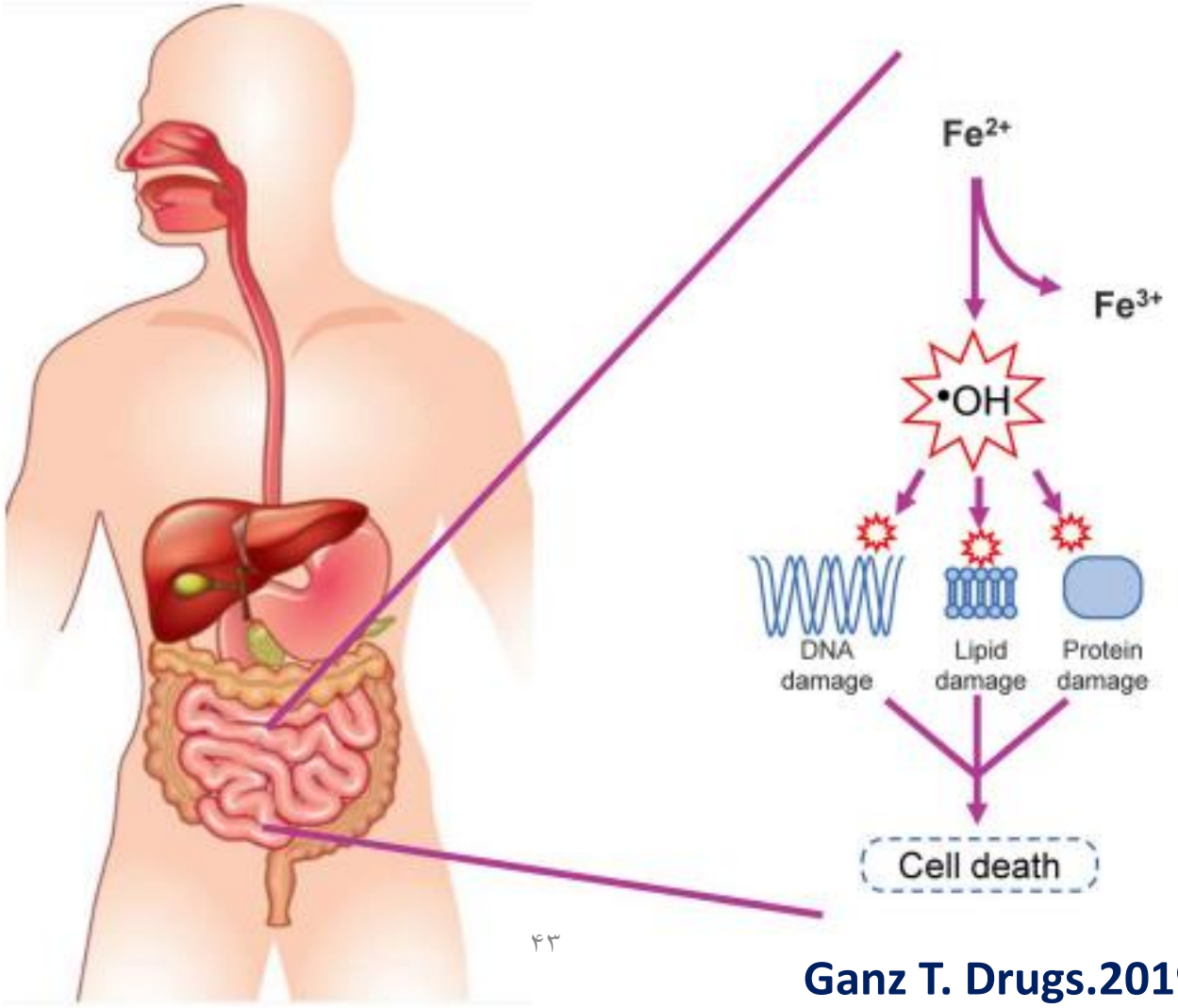
Overview of iron absorption pathway



Ganz T. Drugs.2019

Iron misregulation & generation of reactive oxygen species

- **Ferric iron**, such as in Auryxia & unlike ferrous iron, is **not** easily oxidized.
- **Ferrous iron**, during oxidation, can catalyze the formation of free radicals, causing GI mucosal cell damage & erosions of the GI mucosa.



Ganz T. Drugs.2019

Tenapanor (IBSRELA)

- Tenapanor, an experimental luminal **blocker of Na-H exchange (NHE3)** was recently found to lower paracellular ph transport in the gut as an indirect effect.
- In short term studies sponsored by the manufacturer, tenapanor shows reduction in serum ph over 8 wks in patient on HD of approximately **1 mg/dl** & FGF23 modestly by 10–30%.
- Know, only short term studies are available & tenapanor remains **experimental** & in phase 3 studies.

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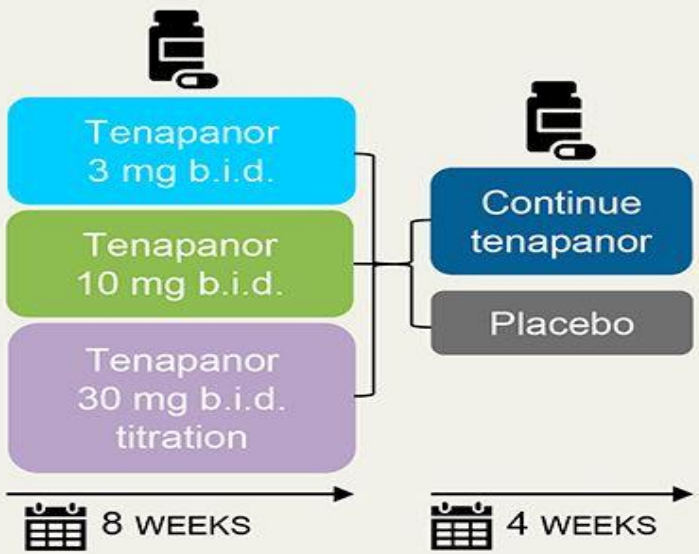
Tenapanor for Patients on Hemodialysis with Hyperphosphatemia: A Randomized Phase 3 Trial

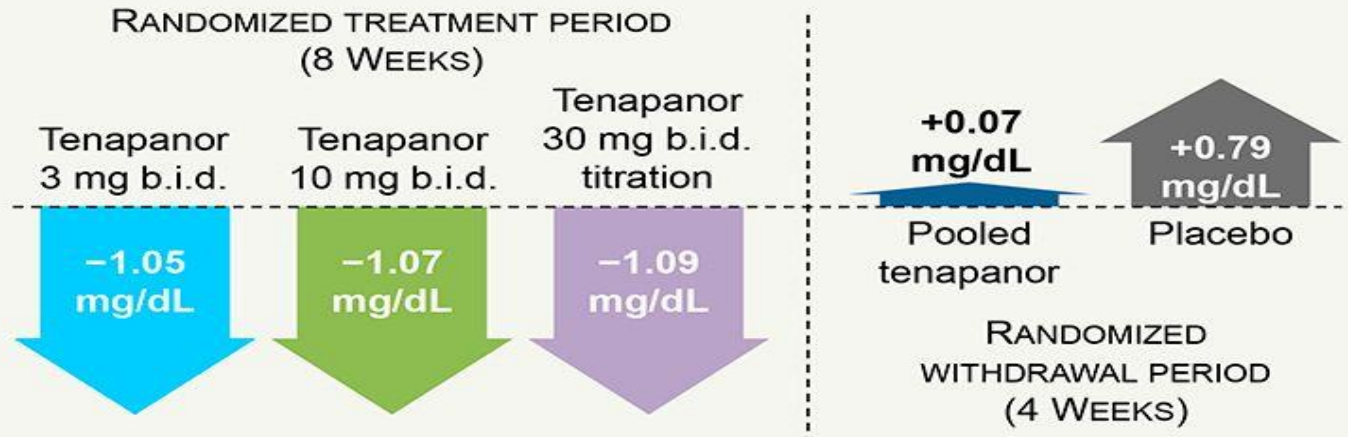
METHODS

219 patients across 41 US sites



RESULTS

Change in serum phosphate



CONCLUSION

Tenapanor significantly reduced elevated serum phosphate in patients on hemodialysis with hyperphosphatemia.

doi: 10.1681/ASN.2018080832

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

Rationale for class selection

1. The desire to restrict ca
2. LDL-lowering & anti-inflammatory effects are well demonstrated for sevelamer-based products
3. Ferric citrate may also treat anemia
4. Sucroferric oxyhydroxyide may provide a lower pill burden
5. Cost
6. Side effects

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Seminars in Dialysis

Reviews

The Phosphate Binder Equivalent Dose

John T. Daugirdas,* William F. Finn,† Michael Emmett,‡ Glenn M. Chertow,§ and the Frequent Hemodialysis Network Trial Group[1]

*University of Illinois at Chicago, Chicago, Illinois, †University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, ‡Baylor University Medical Center, Dallas, Texas, and §Stanford University School of Medicine, Palo Alto, California

ABSTRACT

Phosphate binders include calcium acetate or carbonate, sevelamer hydrochloride or carbonate, magnesium and lanthanum carbonate, and aluminum carbonate or hydroxide. Their relative phosphate-binding capacity has been assessed

sevelamer hydrochloride or carbonate 0.75, for calcium acetate 1.0, for anhydrous magnesium carbonate 1.7, and for "heavy" or hydrated, magnesium carbonate 1.3. Estimated RPBC for aluminum-containing binders were 1.5 for alumi-

Daugirdas JT. Seminars in Dialysis, 2011

Relative Ph-binding coefficient

Phosphate binder	RPBC by g of compound listed in available product
Calcium carbonate (index value)	1.0
Calcium acetate	1.0
Magnesium carbonate (anhydrous weight, Magnebind)	1.7
"Heavy" magnesium carbonate (hydrated weight, OsvaRen)	1.3
Aluminum hydroxide	1.5
Aluminum carbonate	1.9
Sevelamer (carbonate or hydrochloride)	0.75
Lanthanum carbonate	2.0[a]

Take-home Message

- Ca versus non-ca-based binders is now an old, yet **unsettled question** in nephrology.
- In addition, the quality of data available to determine this question is **poor**, characterized by numerous biases highlighted throughout this perspective.
- In our view, data are currently **inadequate** to justify:
  1. Regular use of ph binders in patients with CKD G3–5 (non-dialysis)
  2. Intensive use of binders to specific ph targets in kidney failure
  3. Preference for one class of binders over another.

Julia J. AJKD. 2021


شهادتنامه محمود شهید
۲۱۰