

Forté[™]
Fracture

Science-based, Targeted Nutritional
Support for Optimal Fracture Healing



RECOVER

fracture product

Creating the Optimal Internal Biochemical Environment to Support Fracture Healing

Each year, an average of 6 million people in the United States will break a bone, accounting for 16 percent of all musculoskeletal injuries and more than 3.5 million emergency department visits.¹ In fact, the average citizen in a developed country can expect to sustain two fractures over the course of his or her lifetime. Prior to age 75, the most common site of fracture is the wrist. In those over age 75, hip fractures represent the most common broken bone. By 2025, age–or osteoporosis–related fractures are projected to increase to more than 3 million per year, solely on the basis of growth in the elderly population at risk.²

In response to a bone fracture, the body acts swiftly to initiate healing, as cells in the neighboring tissue send out chemical messengers that encourage the growth of small blood vessels and, eventually, differentiation of mesenchymal stem cells into cartilage, bone, and fibrous tissue.³ While most broken bones heal without incident over time, approximately five to 10 percent of bone fractures fail to heal normally, resulting in delayed healing or non-union.¹

The nutritional stage set for healing can influence the speed, comfort and completeness of the bone renewal process. Substantial clinical research supports the role of nutritional supplementation –including protein, natural antioxidants and anti-inflammatories, minerals, and vitamins–in bolstering and accelerating fracture healing. However, fracture healing is a complex biological process that requires multi-nutrient support and it may be difficult for patients and their physicians to find a high-quality, pharmaceutical-grade supplement that addresses the specific nutritional needs of fracture patients.

Physiology of Fracture Healing^{3,4}

During the last two decades, our understanding of fracture healing has evolved rapidly. Bone is one of the few body tissues that can heal without forming a fibrous scar and, as such, the process of fracture healing recapitulates bone development and may be considered a form of tissue regeneration. The complex cell and tissue proliferation and differentiation processes involved in fracture healing are regulated by growth factors, inflammatory cytokines, antioxidants, hormones, amino acids, and other nutrients.

The process of fracture healing can be divided into three phases:

- **Inflammatory phase**–This first stage of healing begins immediately upon fracture, when a hematoma forms, setting off a cytokine cascade that leads to the influx of macrophages and inflammatory leukocytes into the fracture gap.

1– American Academy of Orthopaedic Surgeons. OrthoInfo: Physical Fields. Available at <http://orthoinfo.aaos.org/topic.cfm?topic=A00279>.

2– Burge R, et al. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005-2025. *J Bone Miner Res* 2007;22:465-475.

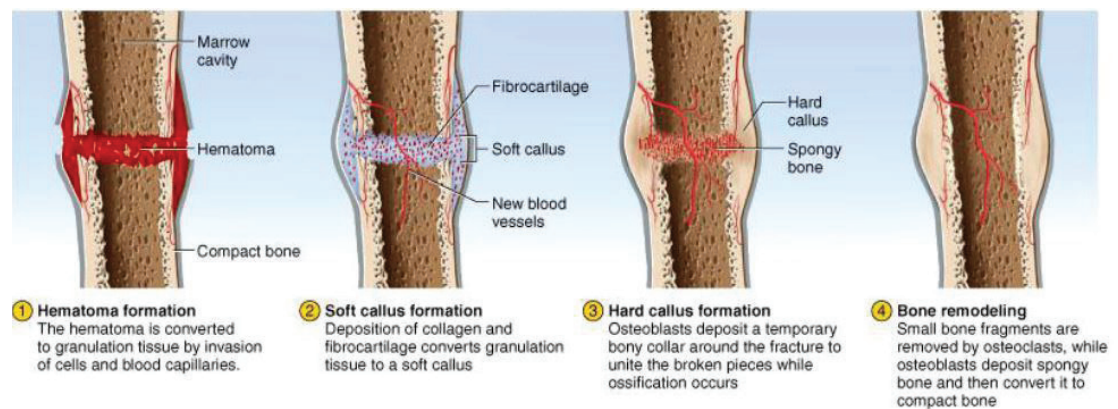
3– Marsell R, Einhorn TA. The biology of fracture healing. *Injury* 2011;42(6):551-555.

4– Marsh DR, Li G. The biology of fracture healing: optimizing outcome. *British Medical Bulletin* 1999;55(4):856-869.

These cells scavenge debris and begin producing the pro-inflammatory agents that initiate healing. Inflammation triggers growth of new blood vessels, as well as differentiation of cells into bone-building osteoblasts and cartilage-forming chondroblasts. Over the next few months, these cells form new bone matrix and cartilage, while osteoclasts break down and recycle bone debris.

- Reparative phase—The second stage of healing begins approximately two weeks after the fracture occurred. During this time, proteoglycans and collagen produced by the osteoblasts and chondroblasts begin to consolidate into a soft callus, which is eventually resorbed and replaced by a hard callus through endochondral ossification and direct bone formation over a six- to 12-week time period.
- Remodeling phase—Although the hard callus is a rigid structure that provides stability, it does not fully restore the biomechanical properties of normal bone. In the final stage of fracture repair, the hard callus matures and remodels into strong, highly-organized lamellar bone with a central medullary cavity, a process orchestrated by osteoblasts and osteoclasts.

Figure 1. Stages of Fracture Healing¹



Source: McGraw Hill

Nutritional Demands of Fracture Healing

Each stage of the fracture healing process is accompanied by increased nutritional demands. The trauma of the fracture itself causes oxidative stress, releasing free radicals that may tax or even overwhelm the body's antioxidant reserves. The fracture healing process also requires significant energy, an adequate blood supply and an ample store of amino acids for new protein synthesis.

Using Nutrition to Support Fracture Healing

Meeting Energy Demand

While a normally active adult requires approximately 2,500 calories a day, a patient with multiple fractures may need up to 6,000 calories per day to meet the energy requirements for healing.² If this demand is not met, the fracture healing process may be compromised.³ Increasing caloric intake to meet increased metabolic demand may help to promote healing.

1- Prentice WE. Principles of athletic training: a competency-Based approach. New York, NY: McGraw-Hill; 2014. highered.mheducation.com/sites/dl/free/0078022649/.../Prentice15e_Chap10.pdf.

2- Smith TK. Prevention of complications in orthopedic surgery secondary to nutritional depletion. Clin Ortho and Related Research 1987;222:91-97.

3- Kakar S, Einhorn TA. Importance of nutrition in fracture healing. In Nutrition and Bone Health, ed. Holick MR and Dawson-Hughes B. Totowa, NJ; Humana Press Inc., 2004.

Assuring Adequate Protein

Protein comprises approximately half of bone by volume. When a fracture occurs, amino acid building blocks are needed to synthesize a new structural bone protein matrix. Amino acids of specific importance for fracture healing include lysine, arginine, proline, glycine, cysteine, and glutamine. For example, lysine is known to enhance calcium absorption, increase the amount of calcium absorbed into the bone matrix, and aid in tissue regeneration. In addition, protein supplementation increases growth factors such as insulin-like growth factor-1 (IGF-1), a polypeptide that exerts a positive effect on skeletal integrity, muscle strength, immune response, and bone renewal.^{1,2}

Protein deficiency leads to a rubbery, rather than rigid, callus. Multiple studies have demonstrated acceleration of fracture healing with even a modest 10- to 20-gram increase in protein intake. Supplemental protein is particularly important in those with low baseline protein intake or protein malnutrition. In fact, among elderly patients with hip fracture, poor protein status at the time of fracture is predictive of fracture outcome. Patients with poor protein status take longer to heal and are more likely to suffer complications, including death.^{3,4,5}

Increasing Antioxidants and Anti-Inflammatories

When a fracture occurs, free radicals are generated by the damaged tissues, particularly as tightly-bound strands of collagen in the mineral phase of bone are snapped. These ruptured collagen strands interact with oxygen, giving rise to free radical metabolites, which are associated with inflammation, further collagen breakdown and excessive bone turnover.⁶ In patients who have sustained bone fracture, increased free radical production may overwhelm the body's natural antioxidant defense mechanisms. Studies in animal models and cultured human cell lines suggest that supplementation with natural antioxidants, including vitamin C, vitamin E, lycopene, and alpha-lipoic acid, may be beneficial in suppressing the destructive effect of free radicals and improving fracture healing.^{1,2}

An essential component of the bone healing process, the initial inflammatory phase that occurs at the time of fracture involves the release of prostaglandins from cells damaged by the trauma of the fracture. Prostaglandin-induced inflammation activates the cyclooxygenase (COX)-1 and COX-2 enzymes, which play important roles in fracture repair. Although standard non-steroidal anti-inflammatory drugs (NSAIDs) might help relieve the pain associated with the fracture and subsequent inflammation, they would also inhibit the action of the COX-1 and COX-2 enzymes and, thus, delay healing. As a result, NSAIDs—including aspirin, ibuprofen, indomethacin, etodolac, meloxicam, nabumetone, and naproxen—are not recommended for

1– Bonjour JP, Schurch MA, Rizzoli R. Nutritional aspects of hip fractures. *Bone* 1996; 18:139S-144S.

2– Schurch MA, et al. Protein supplements increase serum insulin-like growth factor-1 levels and attenuate proximal femur bone loss in patients with recent hip fracture. *Ann Intern Med* 1998;128(10):801-809.

3– Koval KJ, et al. The effects of nutritional status on outcome after hip fracture. *J Ortho Trauma* 1999;13(3):164-169.

4– New SA. The role of the skeleton in acid-base homeostasis. *Proceedings of the Nutrition Society* 2002;61:151-164.

5– Bastow MD, Rawlings J, Allison SP. Benefits of supplementary tube feedings after fractured neck of femur: a randomized controlled trial. *BMJ* 1983;287:1589-1592.

6– Sheweita SA, Khoshhal KI. Calcium metabolism and oxidative stress in bone fractures: role of antioxidants. *Current Drug Metabolism* 2007;8:519-525.

fracture pain relief.^{1,2} However, nourishing the body to reduce inflammation may accelerate healing. Natural anti-inflammatories such as vitamin C, omega-3 fatty acids and quercetin or other bioflavonoids may quiet the inflammatory process and promote healing.

Boosting Mineral Intake

Minerals such as calcium, phosphorous, magnesium, silicon, and zinc account for 70 percent of bone by weight. Fracture healing requires the availability of these minerals. Many patients under-consume minerals on an everyday basis, creating a mineral deficit that is exacerbated in the context of fracture. Key minerals for fracture healing include:

- Zinc—An estimated 200 enzymes require zinc for normal functioning. Zinc supplementation aids in callus formation and enhances production of bone protein, stimulating fracture healing.³
- Copper—Copper is needed for the formation of collagen. Studies have shown that the body's demand for both copper and zinc rises according to trauma severity.⁴
- Calcium and Phosphorus—Calcium and Phosphorus—in the form of calcium hydroxyapatite crystals—are the main minerals in bone. Calcium hydroxyapatite plays a critical role in regulating the elasticity and tensile strength of bone.⁶ The reparative and remodeling phases of fracture healing require adequate supplies of both calcium and phosphorus, which can be obtained first from bone reserves and then from the diet.

Calcium is drawn from skeletal bones during the first few weeks of healing, but further repair requires dietary calcium. While very high intakes of calcium do not appear to speed fracture healing, consuming adequate calcium at the recommended daily allowance (RDA) is important.^{5,6} Calcium absorption is dependent on vitamin D, and studies suggest that calcium and vitamin D should be obtained in optimum daily doses for effective fracture healing.⁷ Phosphorus supplementation should be considered in the elderly, dieters, and those on low protein diets, as these individuals may not consume enough phosphorus to meet the needs of new bone formation.⁸

- Silicon—Bioactive silicon plays an important role in collagen synthesis. A recent study found bioactive silicon enhances the effects of calcium and vitamin D3 on new bone formation.⁹

Getting the Right Vitamins

While protein and minerals are the building blocks for bone, vitamins are the catalysts for many of the biochemical reactions involved in bone repair. In particular, the B vitamins, vitamin C, vitamin D, and vitamin K play vital roles in fracture healing, and should all be taken in therapeutic doses.¹⁰

1- Murnaghan M, Li G, Marsh DR. Nonsteroidal anti-inflammatory drug-induced fracture nonunion: an inhibition of angiogenesis? *J Bone Joint Surg Am* 2006;88 Suppl 3:140-147.

2- Nwadinigwe CU, Anyaehi UE. Effects of cyclooxygenase inhibitors on bone and cartilage metabolism – a review. *Niger J Med* 2007;16(4):290-294.

3- Igarashi A, Yamaguchi M. Great increase in kDa protein and osteocalcin at later stages with healing rat fractures: effect of zinc treatment. *Int J Mol Med* 2003;11(2):223-228.

4- Simsek A, et al. Is there a correlation between severity of trauma and serum trace element levels? *Acta Orthop Traumatol Turc* 2006;40(2):140-143.

5- Key JA, Odell RT. Failure of excess minerals in diet to accelerate the healing of experimental fractures. *J Bone Joint Surg* 1955;37A:37.

6- Singh LM, Della Rosa RJ, Dumphy JE. Mobilization of calcium in fractured bones in rats. *Surg Gynecol Obstet* 1963;126(2):243-248.

7- Doestch A, et al. The effect of calcium and vitamin D3 supplementation on the healing of the proximal humerus fractures: a randomized placebo-controlled study. *Calcified Tissue International* 2004;75(3):183-188.

8- Heaney RP, Nordin BEC. Calcium effects on phosphorus absorption: implications for the prevention and co-therapy of osteoporosis. *J Am Coll Nutr* 2002;21(3):239-244.

9- Spector TD, et al. Effect on bone turnover and BMD in low dose oral silicon as an adjunct to calcium/vitamin D3 in a randomized placebo-controlled trial. Abstract from the ASBMR 27th Annual Meeting 2005, Nashville, TN.

10- Brown SE. How to speed fracture healing. Center for Better Bones, Syracuse, NY.

Vitamin B6

Vitamin B6, one of the B-complex vitamins that has been linked to fracture healing, is thought to modulate the effects of vitamin K on bone through complex biochemical pathways.¹ Animal studies have linked vitamin B₆ deficiency to more frequent fractures, as well as reduced fracture healing.

Vitamin C

In addition to its antioxidant and anti-inflammatory properties, vitamin C is needed for synthesis of the bone collagen protein matrix and severe vitamin C deficiency leads to unstable collagen. In rodent models, vitamin C supplementation accelerates the fracture healing process and higher vitamin C blood levels lead to stronger fracture callus formation.^{2,3} Vitamin C may also help to reduce the likelihood of developing complex regional pain syndrome (CRPS). In a study of 328 wrist fracture patients, supplementation with 500 milligrams per day of vitamin C reduced the incidence of post-fracture CRPS by more than fourfold.⁴

Vitamin D

As the primary regulator of calcium absorption, vitamin D is critical for making calcium available for fracture healing and is an independent predictor of functional recovery following hip fracture.⁵ As far back as 1945, studies demonstrated that low vitamin D levels led to sub-optimal fracture healing and supplementation with vitamin D accelerated initial fracture callus mineralization.^{6,7} Research has also shown that vitamin D—in conjunction with vitamin K—stimulates the transformation of fracture site mesenchymal stem cells into osteoblasts.⁸

Vitamin K

Vitamin K has long been noted to have a beneficial effect on fracture healing.⁹ It plays an essential role in the biochemical processes that bind calcium to bone, and is required for proper formation of osteocalcin, a bone protein. Vitamin K also aids in conserving calcium by reducing the excretion of calcium in urine.¹⁰ Studies have shown that vitamin K is sequestered at the fracture site, resulting in decreased circulating vitamin K levels, and the time needed for vitamin K blood levels to return to normal is influenced by fracture severity.¹¹

A Multi-Nutrient Approach to Fracture Healing

Since bone is a complex tissue that requires many nutrients, supplementation with a wide range of key bone nutrients is likely to provide more effective support for fracture healing than individual nutrient supplementation. Several studies have found that multi-nutrient therapy accelerates fracture healing and reduces complications:

1– Reynolds TM. Vitamin B6 deficiency may also be important. *Clin Chem* 1998;44:2555-2556.

2– Yilmaz C, et al. The contribution of vitamin C to healing of experimental fractures. *Archives of Orthopaedic and Trauma Surgery* 2001;121(7):426-428.

3– Alcantara-Martos T, et al. Effect of vitamin C on fracture healing in elderly Osteogenic Disorder Shionogi rats. *J Bone Joint Surg Br* 2007;89-B(3):402-407.

4– Zollinger PE, et al. Can vitamin C prevent complex regional pain syndrome in patients with wrist fractures? *J Bone Joint Surg* 2007;89:1424-1431.

5– DiMonaco M, et al. Serum levels of 25-hydroxyvitamin D and functional recovery after hip fracture. *Arch Phys Med Rehabil* 2005;86(1):64-68.

6– Copp DH, Greenberg DM. Studies on bone fracture healing I: effect of vitamins A and D. *Jr or Nutr* 1956;29(4):261-267.

7– Steier A, et al. Effect of vitamin D2 and fluoride on experimental bone fracture healing in rats. *J Dent Res* 1967;46(4):675-680.

8– Gigante A, et al. Vitamin K and D association stimulates in vitro osteoblast differentiation of fracture site derived human mesenchymal stem cells. *J Bio Regul Homeost Agents* 2008;22(1):35-44.

9– Bouckaert JH, Said AH. Fracture healing by vitamin K. *Nature* 1960;185:849.

10– Knaper MHJ, Hamulyák K, Vermeer C. The effect of vitamin K supplementation on circulating osteocalcin (bone G1a protein) and urinary calcium excretion. *Ann Intern Med* 1989;111:1001-1005.

11– Bitensky L, et al. Circulating vitamin K levels in patients with fractures. *J Bone Joint Surg Br* 1988;70(4):663-664.

- In one clinical study, hip fracture patients who were given complex multi-nutrient supplementation containing carbohydrates, protein, amino acids, sodium, potassium, calcium, magnesium, chloride, trace minerals, and fat-soluble vitamins had a 15 percent rate of complications, as compared to a 70 percent rate of complications among non-supplemented hip fracture patients.¹
- In another placebo-controlled study, tibial fracture patients given a combination of vitamin B6, vitamin C, lysine and proline experienced more rapid fracture healing, with 33 percent of supplemented patients healing in 10 weeks, as compared to only 11 percent in the placebo group.²
- A meta-analysis of 17 clinical hip fracture trials reported that oral multi-nutrient supplementation, including nutrients such as carbohydrates, protein, zinc and antioxidants, reduced hip fracture-related mortality, and complications by nearly 50%.³

Meeting the Nutritional Needs of Fracture Patients

Forté Elements is pioneering the development of condition-specific combinations of vitamins, minerals, amino acids, and other nutrients to support recovery and revitalization. To that end, Forté Elements has developed a multi-nutrient, Medicetual-grade Fracture Drink that helps create a health-promoting internal biochemical environment which conserves bone-building minerals and proteins and supports fracture healing.

In addition to a combination of vitamins, minerals, amino acids, and trace elements shown to accelerate fracture healing, the Forté Elements Fracture Drink contains quercetin—a phytoflavonoid with antioxidant and anti-inflammatory properties—which also seems to have a synergistic effect with vitamin C in reducing fracture-related pain.⁴ The drink also contains bromelain, a proteolytic pineapple enzyme, which has shown value in reducing inflammation, edema and pain in fracture patients.⁵

Forté Elements Fracture Drink

The Forté Elements Fracture Drink may be combined with a physician- or physical therapist-prescribed regimen of joint loading, range of motion and other exercises to accelerate fracture healing and return to function.⁶ Bone tissue responds to patterns of joint loading by increasing matrix synthesis, as well as altering its composition, organization, and mechanical properties. Evidence indicates that this holds true for bone under repair, as well.^{7,8} In addition, exercise enhances circulation, increasing the flow of nutrient-replenishing blood to the fracture site.

The multi-nutrient support provided by the Forté Elements Fracture Drink provides the essential protein, natural antioxidants and anti-inflammatories, minerals, and vitamins needed for fracture healing, and may even be useful in preventing future fractures by ensuring bone health and integrity.

1– Eneroth T, Olsson UB, Thorngren KG. Nutritional supplementation decreases hip fracture-related complications. *Clin Ortho and Related Res* 206;451:212-217.

2– Jamdar S, et al. Reduction in tibial shaft fracture healing time with essential nutrient supplementation containing ascorbic acid, lysine and proline. Letter to the Editor. *J Alter and Comp Med* 2004;10(6):915-916.

3– Cederholm T, Hedström M. Nutritional treatment of bone fracture. *Curr Opin Clin Nutr Metab Care* 005;8(4):377-381

4– Brown SE. How to speed fracture healing. Center for Better Bones, Syracuse, NY.

5– Kamenicek V, Holán P, Franěk P. Systemic enzyme therapy in the treatment and prevention of post-traumatic and postoperative swelling. *Acta Chir Orthop Traumatol Cech* 2001;68(1):45-49.

6– Grundnes O, Reikerås O. Mechanical effects of function on bone healing. Nonweight bearing and exercise in osteotomized rats. *Acta Orthop Scand* 1991;62(2):163-165.

7– Buckwalter JA, Grodzinsky AJ. Loading of healing bone, fibrous tissue and muscle: implications for orthopaedic practice. *J Am Acad Orthop Surg* 1999;7(5):291-299.

8– Zhang P, Malacinski GM, Yokota H. Joint loading modality: its application to bone formation and fracture healing. *Br J Sports Med* 2008;42(7):556-560.



What is a Medicetical?

A Medicetical is a pharmaceutical-grade nutritional support system designed for a specific medical condition using clinically proven ingredients that are based on published science. In conjunction with licensed physicians, Forté Elements has defined and developed rigorous standards for the emerging Medicetical category.

In order to meet the criteria for a Medicetical, a nutritional supplement must:

1. Be formulated to support a specific health condition or situation
2. Contain only non-synthetic, pharmaceutical-grade ingredients that are Generally Recognized as Safe (GRAS)
3. Contain elements that have been validated by clinical research for the specific health condition or situation, as published in peer-reviewed journals
4. Conform to pharmaceutical-grade dosage standards for the specific health condition or situation
5. Be produced in FDA-compliant manufacturing facilities using pharmaceutical-grade manufacturing practices
6. Product has a Certificate of Analysis available confirming that product ingredients meet the Medicetical standard and are as listed on the product label.

Supplement Facts

Serving Size 1 Pack (57 Grams)
Servings Per Container 30

Amount Per Serving

	% Daily Value*
Calories 125	6%
Total Fat 1g	2%
Total Carbohydrate 8g	3%
Dietary Fiber 1g	4%
Protein 15 g	30%
Vitamin A (Beta-Carotene and Acetate) 3500 IU	70%
Vitamin C (Calcium Ascorbate) 1500mg	2500%
Vitamin D (Cholecalciferol) 2000 IU	500%
Vitamin E (d-Alpha Tocopheryl) 50 IU	167%
Vitamin K (Fat Soluble) 100mcg	125%
Vitamin B1 (Thiamin) 100mg	6666%
Vitamin B2 (Riboflavin) 10mg	588%
Vitamin B3 (Niacin) 20mg	100%
Vitamin B6 (Pyridoxine) 10mg	500%
Folic Acid 400mcg	100%
Vitamin B12 (Cyanocobalamin) 100mcg	1667%
Biotin 80mcg	27%
Pantothenic Acid 20mg	200%
Calcium 2000mg	200%
(Carbonate, Lactate, Phosphate, Ascorbate)	
Iron (Gluconate) 18mg	100%
Phosphorus (Calcium Phosphate) 1000mg	100%
Iodine 150mcg	100%
Magnesium (Hydroxide) 200mg	50%
Zinc (Gluconate) 25mg	167%
Selenium 70mcg	100%
Copper (Gluconate) 2mg	100%
Manganese (Gluconate) 5mg	250%
Chromium (Polynicotinate) 50mcg	42%
Sodium 200mg	8%
Potassium 80mg	2%

Proprietary Blend 10.3g

**
Strontium Citrate, Taurine, L-Arginine, Oat Bran Fiber, L-Lysine, Horsetail Silica, Glycine, L-Proline, Glucosamine HCL, Quercetin, Alpha Lipoic Acid, Bromelain, Coenzyme Q10, Chondroitin Sulfate, Boron

*Percent Daily Values are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs.
**Daily Value not established.

OTHER INGREDIENTS: WHEY PROTEIN CONCENTRATE, SWEET WHEY, COCOA POWDER, CITRIC ACID, NATURAL VANILLA FLAVOR, STEVIA (NON-NUTRITIVE SWEETENER). **CONTAINS:** MILK AND CRUSTACEAN SHELLFISH.

WARNING: ACCIDENTAL OVERDOSE OF IRON-CONTAINING PRODUCTS IS A LEADING CAUSE OF FATAL POISONING IN CHILDREN UNDER 6. KEEP THIS PRODUCT OUT OF REACH OF CHILDREN. IN CASE OF ACCIDENTAL OVERDOSE, CALL A DOCTOR OR POISON CONTROL CENTER IMMEDIATELY.

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