

# MuscleDefender

# Goal

To supply L-glutamine in a stable patented dipeptide form (magnesium glycyl glutamine chelate) in order to greatly improve oral L-glutamine supplementation's ability to function as an effective immuno-nutrient and in its many other important roles in cell growth and survival during times of depletion brought on by demanding stresses. Replenishing glutamine during times of depletion caused by rapid growth, tissue repair or other high metabolic demands, particularly when combined with prolonged energy restriction, may help to maintain health (immune support) including the integrity of the intestinal tract and enhance recovery as compared to a non-supplemented state.

# Rationale

Glutamine is the amide (an amide is any functional group containing a carbonyl group linked to a nitrogen atom) of glutamic acid, and is uncharged under all biological conditions. Glutamine is the most abundant free amino acid (AA) in the body (up to 50% of the free AA pool in the blood and skeletal muscle).<sup>1,2,3</sup> It is produced primarily in skeletal muscle and then released into the circulation.<sup>4</sup> Tissues that require glutamine such as the immune system, gastrointestinal tract, kidneys, and liver obtain glutamine as needed from the blood.<sup>5</sup> Academically classified as a nonessential amino acid (NEAA), glutamine is essential for maintaining intestinal function, amino acid homeostasis and immune response during severe stress, therefore generally referred to as a conditionally essential amino acid.<sup>4,5</sup> Glutamine's unique structure makes it a universal precursor in high demand. The amino acid can be used as fuel (anaplerotic substrate especially in rapidly proliferating tissues),<sup>4</sup> a substrate for nucleotide synthesis, a modulator of intermediary metabolism of amino acids,<sup>6,7</sup> and a component of GSH (y-glutamyl-cysteinyl-glycine)-mediated antioxidant defense,<sup>8</sup> and therefore a primary substrate for cell survival, maintenance and proliferation.<sup>4,9</sup> Glutamine also serves as an osmolyte in regulating cell homeostasis in hyper and hypo-osmolar conditions through cell shrinkage and swelling, conditions that may play a role in the regulation of protein synthesis.<sup>10,11</sup> Because of the many important functions of glutamine (see below), there is a dramatic increase in the net release of glutamine from peripheral tissues, including muscle, to central tissues (e.g. liver, immune system, etc.) during inflammatory and other physically stressful conditions,<sup>4</sup> giving rise to the basis of supplementation during clinical (trauma, infection, wound healing, etc.) and non-clinical (intense prolonged exercise) situations.<sup>4,12</sup>

Functions of Glutamine 4,9 (additional references below in Mechanisms of Action section)

- Substrate for protein, citrulline and arginine synthesis
- Ammonia scavenger
- Nitrogen donor and transport mechanism
- Shuttle for glutamate for the central nervous system
- Substrate for glutathione production and redox balance (NADPH production)
- Stimulates glycogen synthesis
- Substrate for hepatic ureagenesis and hepatic and renal gluconeogenesis
- Participates in acid-base balance
- Fuel for intestinal enterocytes
- Nucleic acid precursor and involved in generation of cytotoxic substances in immunocompetent cells
- Involved in cell volume through osmotic signaling potentially related to protein synthesis and injury

# **Mechanism of Actions**

A very brief overview of glutamine metabolism helps understand its proposed mechanisms of action. Glutamine is readily transported into cells and deamidated (removal of amide functional group) in several tissues (intestine, liver, spleen, immune cells, and kidney) to yield glutamate and NH3.<sup>6,7</sup> Subsequently, glutamate is either



transformed to α-ketoglutarate via its dehydrogenase or transaminated (transfer of an amino group from one compound to another) to also yield α-ketoglutarate, which serves as an intermediate in the Krebs cycle (KC). In this pathway, glutamine serves as an anaplerotic substrate, replenishing Krebs cycle intermediates in rapidly proliferating tissues.<sup>6,7</sup> However, in these tissues, the intermediates may only be partly regenerated because they branch off at several sites of the KC to supply substances supporting cell proliferation in the immune response, wound repair, and growth and to maintain redox (reduction–oxidation reaction) balance.<sup>6</sup> KC intermediates must be replenished (anaplerosis) to allow this branching off, which is accomplished primarily by glucose –derived pyruvate.<sup>7</sup> These back and forth processes increase exponentially during high inflammatory or growth rates thus rapidly depleting glutamine availability.<sup>4</sup>

Summarizing the glutamine (GLN) pathways in the stressed/injured host: after intramuscular synthesis of glutamine and alanine, peripheral proteins including skeletal muscle are broken down to deliver amino acids (AA) to the systemic circulation. They may now be converted to glucose to supply the carbon skeleton for the resynthesis of glutamine, alanine or other non-essential AAs in peripheral tissues for the biosynthetic need of healing tissues and/or to produce the reduced form of nicotinamide adenine dinucleotide phosphate (NADPH) for maintenance of the redox potential.<sup>4</sup> It has been postulated that there is a synergistic necessity for glutamine and glucose in order for immune and other rapidly proliferating cells to function optimally. The synergistic demand would be driven by the need for NADPH, which is also necessary for molecules required for pinocytosis (fluid transport) and phagocytosis (foreign matter removal) both actions important in the immune processes.<sup>13,14</sup> See list below for the proposed mechanisms of action that support GLNs role in cell survival, proliferation and maintenance.

At least in a clinical sense, it can be concluded that in an under diseased or traumatized host, or during rapid growth situations, glutamine plays an essential role in producing substrate for the pathways operative in these conditions.<sup>4,12,15</sup> Considering GLN's role in intermediary metabolism, any shortage in glutamine availability would suggest that flux in most of these biosynthetic and redox-regulating processes would be compromised. GLN shortages would be especially harmful in conditions where rapid cell proliferation and immune defenses are required, giving rise to supplementation.<sup>4,12,15,16,17</sup>

#### Potential Mechanisms of Glutamine to Support Stress Related Bodily Harm<sup>4,12</sup>

- Anti-inflammatory/immune regulation by attenuating: 1) activation of nuclear factor-κB and cytokine release and
   2) decreases in immune cell function, including neutrophils and lymphocytes
- Increase tissue concentration of GSH attenuating oxidative stress
- Provision of NADPH (stimulating intermediary metabolism and preventing apoptosis by supporting mitochondria function) to increase neutrophils and lymphocytes activity and function
- Preservation of tissue functions via maintenance of ATP levels
- Promotion of intestinal integrity<sup>18</sup>
- Activates heat shock factor 1 (HSF-1). Tissue protection from enhanced heat shock expression by activating nutrient receptors (sirtuin 1/human antigen R) leading to the activation of heat shock transcription factor in the nucleus favoring cell survival<sup>8,19,20</sup>
- Glutamine availability is a limiting step for the mTOR complex 1 activation pathway, a primary control point for cell size including skeletal muscle<sup>21</sup>

Considering all the above, the goal would be to supplement the approximate amounts of glutamine released by the peripheral tissues during added stress (at least in the incremental difference from release under normal conditions) in order to help maintain a physiological environment more conducive to recovery and maintenance of health. Putatively, as opposed to a non-supplemented state where stores of glutamine would have to be released, setting off a triage type situation in order to favor survival over short term health, supplementing glutamine would help offset otherwise resulting damage. It is this theory that has brought glutamine supplementation to the world of exercise and



sport since activity depending on intensity, duration, individual physiological state and energy balance, can bring on many of the outward conditions described above including compromising intestinal<sup>22</sup> and immune system integrity.<sup>12</sup>

# **Glutamine in Exercise and Sport**

While glutamine's mechanisms of action and clinical success using supplementation as described above makes glutamine an attractive supplement for athletes, the evidence at this time supporting benefits is equivocal at best and probably explains why it's generally a no-show on expert's list of effective dietary supplements for healthy athletes.<sup>23,24</sup> That said, glutamine supplementation has survived the test of time for many athletes that continue to use it during intense training and long duration activities, and/or for competitions, believing it helps recovery and immune function, especially when combined with severe or prolonged energy restriction.<sup>25</sup> An explanation for the aforementioned phenomenon may be that athletes who perceive success may, through their specific diets and activities, actually deplete enough glutamine stores or surpass endogenous glutamine's ability to function optimally in respective protective pathways. Additionally, when L-glutamine is ingested in its free form, the amino acid is largely metabolized in the rapidly reproducing gut tissues, <sup>26,27</sup> potentially leaving less available for other tissues, including immune cells.<sup>28</sup> To avoid this fate and to increase glutamine's potential effectiveness in other target pathways (e.g. glutathione synthesis, immune, heat shock and anabolic signaling, etc.), glutamine is often supplied in a dipeptide form (attached to another amino acid) such as alanine or glycine, which is currently now common in clinical practice.<sup>29,30,31,32,33,34,35</sup> Although free form and dipeptides both have been shown to raise plasma glutamine concentrations within two hours,<sup>36,37</sup> in the dipeptide form, glutamine remains highly soluble and stable and may achieve higher levels into circulation because of the glycopeptide transport protein (PepT-1) in the enterocytes having greater efficiency in transporting small peptides for absorption than free form AAs.<sup>38</sup> In this sense, the form in which glutamine supplementation is ingested may also be a factor in potential desired (or claimed) efficacy – i.e. reaching target tissues in greater amounts.<sup>39</sup>

## **Glutamine Studies in Sport & Exercise**

It should be noted that earlier studies found the oral dosage of L-glutamine that may attenuate the exercise induced decrease in plasma glutamine and lymphocytes, thus lower the risk of URT1s,<sup>36</sup> was approximately ~0.05 g/lb of body weight (10 g for a 200 lb person).<sup>17,40</sup> Other studies using fixed (20-30 g/day) or higher dosages (0.14-.023 g/lb) found contrary results.<sup>41</sup> The latter may be from the conditions mentioned above. Sticking with the above stated goal of glutamine supplementation supporting the immune system and recovery during intense prolonged training regimens, below are related clinical trials.

- Agostini F. et al. investigated the effect of physical activity on glutamine metabolism and suggested that following
  exercise, the reduced glutamine availability may be a marker of overreaching, thus supplementation may decrease
  inflammation and enhance otherwise compromised immunocompetence after strenuous activity.<sup>42</sup>
- Sasaki E et al. tested 3000 mg/day of glutamine supplementation on neutrophil function in 26 judoists during two weeks of intense training. Results were that the glutamine supplemented group prevented excessive muscle damage and suppression of neutrophil function, especially in reactive oxygen species (ROS) production activity during the strenuous training period.<sup>43</sup>
- Ga Hee Koo, et al. had subjects perform 2000 meters of rowing at high intensity and take three different tests following completion on three separate occasions: using placebo, branched chain amino acids (3.15 g/day), and glutamine (6 g/day) separately in each test. They found that compared with the placebo, groups supplemented with BCAAs or glutamine showed a lower level of blood phosphorous during the recovery stage after maximal intensity exercise. The glutamine group alone appeared to have a lower concentration of blood creatine kinase, (CK) suggesting positive effects on reduction of stimulating fatigue factors. Differences in measurements of blood IL-6 and IL-15 were found between the resting stage and the end of exercise in both placebo and BCAA groups but not in GLN only test groups. The authors conclusions were that glutamine supplementation could be helpful for enhancement of immune function and the defensive inflammatory reaction after exercise.<sup>44</sup>



- Song QH, et al. had athletes performing heavy training loads for 6 weeks during which time the experimental group took 10 g of glutamine orally once a day at three weeks following initial testing while athletes in the control group were given a placebo. Immune function was assessed by measuring the following immunity markers: CD4 and CD8 T cell counts, serum IgA, IgG, and IgM levels, and natural killer (NK) cell activity both before and after the completion of training. While there were no observed differences in serum IgA, IgG, or IgM levels, all other tested levels in the experimental group were positively affected, leading to the conclusion that "glutamine supplementation may be able to restore immune function and reduce the immunosuppressive effects of heavy-load training".<sup>45</sup>
- Rahmani et al. found that glutamine administered daily at .045 g/lb of body weight had no effect on muscle injury markers following six sets to exhaustion of eccentric leg extensions at 75% of 1RM. However, glutamine supplementation appeared to attenuate delayed onset muscle soreness (DOMS).<sup>46</sup>
- Legault et al. tested the effects of glutamine (GLN) and placebo supplementation on quadriceps muscle strength and soreness ratings following exhaustive eccentric exercise. The GLN group used .136 g/lb/d of GLN with equal maltodextrin. The placebo was isocaloric at .272 g/lb/d. L-glutamine resulted in greater relative peak torque both immediately after (71 vs. 66%), and 72 hr. (91 vs. 86%) post-exercise. In the entire sample (men and women), L-glutamine resulted in lower soreness ratings at 24 (2.8 vs. 3.4), 48 (2.6 vs. 3.9), and 72 (1.7 vs. 2.9) hours post-exercise. The authors concluded, "GLN supplementation resulted in faster recovery of peak torque and diminished muscle soreness following eccentric exercise. The effect of L-glutamine on muscle force recovery may be greater in men than women."<sup>47</sup>
- It is well known that intense exercise is associated with an increase in intestinal permeability, also known as "leaky gut," and can lead to negative inflammatory responses.<sup>48,49</sup> Micah N. Zuhl et al. tested the effects of seven days of 0.4 g/lb/d/fat free mass of glutamine supplementation vs. placebo on exercise induced gastrointestinal permeability and tight junction (TJ) protein expression (up-regulation of heat shock response/ HSF-1 activation). Supplementation raised plasma glutamine levels 128%. They found that glutamine supplementation in response to exercise stress: 1) prevented exercise-induced intestinal permeability; 2) enhanced the peripheral blood mononuclear cells (PBMC) level IκBα (suggesting a blunted inflammatory response; 3) increased HSF-1 and HSP70 in response to heat; 4) preserved the stability of occludin (normally declines with heat) at the TJ. The authors suggested the protective effects of glutamine on the gut during vigorous exercise may be multi-pronged: 1) through preserving the intestinal TJ barrier and reducing permeability; and 2) via modulation of the inflammatory response through activation of HSP70 and cytosolic housing of NF-κB thus inactivating its pro-inflammatory pathway.<sup>22</sup>
- Favano et al. used 50 g of maltodextrin (carbohydrate [CHO]) combined with glutamine peptide (CHO/GP) supplying 3.5 g of glutamine vs. 50 g of CHO alone and given 30 minutes before the event, to investigate potential soccer performance enhancement. The conclusion was that the CHO/GP increased athletes' distance and duration of tolerance to intermittent exercise, and lowered feelings of fatigue in players compared to CHO alone. Thus, supplementation with both carbohydrate and peptide glutamine improved the physical performance of these soccer players.<sup>50</sup>

## Dipeptides

As described above, glutamine supplementation may work better in a dipeptide form such as when combined with alanine (or glycine) due to a combination of greater stability (especially in low pH)<sup>29</sup> and an enhanced rate of absorption via specific ion transporters within intestinal epithelia.<sup>51</sup> Furthermore, acute ingestion of an alanine-glutamine dipeptide (AG) has demonstrated an enhanced fluid uptake and attenuation of performance loss during exercise to exhaustion under hypo-hydrated conditions compared to water alone.<sup>52</sup>

• Hoffman et al. examined the efficacy of L-alanyl-L-glutamine (AG) ingestion on basketball performance, including jump power, reaction time, shooting accuracy and fatigue. Female basketball players participated in four trials, each consisting of a 40-minute basketball game with controlled time-outs for rehydration. The first trial (DHY)



subjects were not allowed to rehydrate and the weight lost was used to establish fluid replenishment during the next three trials. In one trial participants consumed only water (W), while during the other two trials subjects consumed the AG supplement mixed in water using either a low dose of 1 g/500 ml for a total of 6 g AG (AG1) or high dose of 2 g/500 ml –total 12 g AG (AG2) concentration. The results showed subjects in the DHY trial lost 2.3% of body mass. No differences in fluid intake were seen between rehydration trials. A 12.5% difference in basketball shooting performance was shown between DHY and AG1 and an 11.1% difference between AG1 and W. Visual reaction time was significantly greater following AG1 compared to DHY. Differences in fatigue, determined by player loads, were seen only between AG2 and DHY. No differences noted in peak or mean vertical jump power during any trial. Authors concluded that rehydration with AG appears to maintain basketball skill performance and visual reaction time to a greater extent than water alone.<sup>53</sup>

- In the same vein as Hoffman et al., McCormack et al. examined the use of I-alanyI-I-glutamine (AG) in a sports drink versus a sports drink alone on time to exhaustion and physiological measures during prolonged endurance exercise. Twelve endurance-trained men performed four trials, each consisting of a one-hour treadmill run at 75% VO<sub>2</sub> peak followed by a run to exhaustion at 90% VO<sub>2</sub> peak. The first trial was with no hydration (NHY); the second consisted of ingestion of only a sports drink (ED); the third utilized allow dose of AG (LD) of 300 mg/500ml, and the fourth trial utilized a high dose of AG (HD) with 1 g/500ml added to the sports drink. During the fluid ingestion trials, 250 ml was consumed every 15 minutes giving a total of 600 mg AG in LD and 2 g in HD. Time to exhaustion was significantly longer during the LD and HD trials compared to NHY, while there were no differences in time to exhaustion between ED and NHY. Plasma glutamine concentrations were significantly elevated at 45 minutes in LD and HD trials and remained elevated at 60 minutes during HD. At 60 minutes, plasma sodium was significantly lower in all trials compared to NHY. These results indicate that even a relatively low dose consumption of an alanine-glutamine dipeptide can significantly improve time to exhaustion during high-intensity exercise compared to a sport (electrolyte) drink alone.<sup>54</sup> Pruna GJ, et al. using the same dosages and basic testing protocol found similar results related to upper and lower body reaction time following exhaustive exercise.<sup>55</sup>
- Mahdi Khorshidi-Hosseini, et al. tested glutamine peptide supplementation with the carbohydrate maltodextrin (CHO), without, and CHO alone on its ability to prevent anaerobic power decrease in repeated competitions. The four groups in this trial were as follows: 1) G group GLN at .11 g/lb body mass), 2) M group 50 g of maltodextrin, 3) GM group 50 g of maltodextrin + GLN at .11 g/lb body mass and, 4) Placebo 250 ml of water and 30 g sweetener. Each participant performed Running-based Anaerobic Sprint Tests (RAST) three times with intervals of one hour. Max power, minimal power (min power) and fatigue were assessed for each subject. The study demonstrated that acute supplementation of GLN peptide with CHO taken two hours before exercise is more efficient in prevention of anaerobic power decrease than placebo, pure carbohydrate or glutamine alone in repeated bouts of RAST protocol, thus improved performance.<sup>56</sup>
- In a pilot study, de Souza et al. tested 30 g/day for 14 days of oral GLN supplementation for its ability to favorably modify the gut microbiota composition in overweight and obese adults. The outcome was that the GLN group had altered the composition of the gut microbiota in overweight and obese subjects, reducing the Firmicutes to Bacteroidetes ratio (biomarker for obesity), resembling the results of weight loss programs currently seen in science.<sup>57</sup>

# **Dosing and Composition**

It is clear that both oral ingestion of free form and peptide glutamine supplementation can raise the body's glutamine levels with the edge going to the more stable and soluble peptide form (glycine or alanine in combination with glutamine) for greater amounts to reach the systemic circulation.

Amounts that have yielded positive results in supporting the immune system, intestinal integrity and recovery related to exercise-induced stresses, range from approximately 5 to 40 g (or .05-0.2 g/lb of body weight) taken always before and sometimes split before, during and after exercise. Based on the rapid depletion of endogenous glutamine during prolonged demanding stress, logically the higher doses may be more appropriate and especially during extended



periods of energy restriction as in weight/fat conscious athletes attempting to "make weight" or achieve extremely low body fat. All considered, suggested dosing may be 0.1 g/lb of body weight split three times daily with half the dose 40 minutes before the exercise, a quarter of the dose immediately following, and the last quarter spaced at least eight hours from other doses, in order to get full daily coverage. For example, a 175 lb athlete would use ~18 g/day (0.1 g X 175 lb) of a dipeptide (e.g. glycyl-glutamine chelate) form of glutamine with activity taking place at 8:00 AM:

- 9 g (1/2 of daily dose) at 7:20 AM (with pre-workout protein and carbohydrate formula/shake)
- 4.5 g (1/4 of the daily dose) immediately following activity
- 4.5 g (1/4 of the daily dose) before bed or mid-evening

*Note:* long duration activities (>3 hours) or continuous daily bouts with intermittent rest periods may require dosing during the span of all activities.

## Safety

As for all amino acids, there is no Upper Limit (UL) established for glutamine. Chronic use of very high doses (>30 g/day), as often used because of clinical necessity, may have negative side effects especially in clinically dependent subjects.<sup>58</sup> However, a systematic review assessing safety and efficacy for chronic high doses (30 g/day) used in cancer patients found side effects similar to control groups.<sup>59</sup> Large doses used in exercise-related studies have reported no toxicity but use should be restricted to intense training periods that may be cycled strategically throughout a competitive season/year.<sup>12,22</sup>

## **Data Summary**

Glutamine (GLN) is the most abundant amino acid in the human body and central to the maintenance and growth of tissues. GLN is rapidly depleted during demanding stresses as it works to activate cell survival and support rapid growth, which would otherwise compromise the host's ability to recovery from injury, sickness or other intense physical stressors. GLN shortages or lack of availability would be especially harmful in conditions where rapid cell proliferation and immune defenses are required. Because of the many important functions of glutamine, there is a dramatic increase in the net release from peripheral tissue (including muscle) to central tissues (e.g. liver, immune system, etc.) during inflammatory and other physically stressful conditions, giving rise to the basis of supplementation during prolonged intense exercise. The goal would be to supplement the approximate amounts of glutamine released by the peripheral tissues during added stress (at least in the incremental difference from release under normal conditions) in order to help maintain a physiological environment more conducive to recovery and maintenance of health including support of immune and intestinal function.

Dosing with a dipeptide (such as glycyl-glutamine) at approximately 0.1 g/lb of body weight split three times daily with half the dose 40 minutes before the exercise, one quarter of the dose immediately following, and the last quarter spaced at least eight hours from other doses in order to get full daily coverage, may have the highest potential to achieve the stated goals. Supplementation may be especially important when prolonged energy restriction (dieting) is combined with demanding physical stresses.

# dotFIT MuscleDefender (MD)

As described throughout this section, the dipeptide form of glutamine is more stable and soluble than its free form counterpart,<sup>29,30,32,33,35</sup> allowing evasion of normal enterocyte extraction and potentially more glutamine (GLN) to reach systemic circulation and other important target tissues.<sup>38,39</sup> Additionally, glutamine in Muscle Defender is bound to a bioavailable magnesium amino acid (glycine) chelate molecule to help maintain GLN stability while avoiding gastric distress.<sup>60</sup> The resulting chelate contains one magnesium cation bonded to one mole of glycine and one mole of glutamine. The final product contains 10% magnesium, 60% glutamine, and 30% glycine. In this form, the glutamine



becomes stabilized to significantly increase plasma levels (see Figure 1) and the magnesium remains bioavailable (remains intact through the gut).<sup>60,61</sup>

At the very least, the MuscleDefender is a high dose NSF Certified for Sport (NSFCS) glutamine supplement with the ability to raise glutamine levels in the gut and overall circulation. However, compared to other GLN products/sources, MuscleDefender's patented form and novel recommendation for use may deliver greater efficacy potential by improving GLN overall availability to desired protective and anabolic pathways described throughout this article and may help explain user's loyalty.<sup>25</sup>

#### **Figure 1 - Glutamine Levels After Ingestion**



MuscleDefender utilizes a patented stabilized form of L-Glutamine that has been demonstrated to elevate plasma and muscle glutamine levels after ingesting; levels then remain elevated above baseline for at least 90 minutes.<sup>60,61</sup>

# **Typical Use**

- Athletes and exercisers under prolonged demanding physical stress, and especially combined with extended periods of energy restriction as in weight/body fat conscious athletes attempting to "make weight" or attain extremely low body fat
- Anyone attempting to support the immune system, intestinal integrity and/or recovery related to
  exercise/physical-induced stresses including to reduce the likelihood of overtraining/reaching or attenuate its
  general effects
- Taking approximately 0.1 g/lb of body weight split three times daily with half the dose 40 minutes before the exercise, one quarter of the dose immediately following, and the last quarter spaced at least 8 hours from other doses in order to get full daily coverage, may have the highest potential to achieve the stated goals. Example of 175 lb athlete: ~18 g/day with activity taking place at 8:00 AM:
  - 9 g at 7:20 AM (with pre-workout protein and carbohydrate formula/shake)
  - 4.5 g immediately following activity (ex: 11:00 AM)
  - 4.5 g before bed or mid-evening
- Long duration activities (>3 hours) or continuous daily bouts with intermittent rest periods may require dosing during the span of all activities



#### **Precautions**

Presently, insufficient data exists to use the risk assessment model for determining an upper limit (UL) for any of the amino acids including glutamine. Furthermore, it is orally well tolerated even in high doses for healthy exercisers.<sup>12,22</sup> As with any amino acid supplementation, individuals with liver or kidney disease should avoid supplementation without supervision of a medical professional.<sup>62</sup>

#### Contraindications

Glutamine supplementation is contraindicated in those with kidney problems or at risk for kidney disease because of possible increased kidney stress.<sup>63</sup> Unless supervised by a qualified health professional, glutamine supplementation should be avoided by children and pregnant or lactating women because of the lack of studies done in these populations. Any persons using anticonvulsants, (or any drug used for epilepsy)<sup>64</sup> and Lactulose should avoid glutamine supplementation. Theoretically, glutamine might antagonize the anti-ammonia effects of lactulose because glutamine can be metabolized to ammonia.<sup>65</sup>

#### **Adverse Events**

Doses up to 40 grams/day of glutamine supplementation have not shown any significant adverse effects.<sup>66</sup> Significant side effects have not been reported in clinical studies.<sup>12,22,58,59,65</sup>

## **Upper Limit (UL)/Toxicity**

Currently, glutamine does not have an established upper limit and has not been shown to elicit toxic effects in high amounts.<sup>64,65</sup>

## **Summary**

#### Purpose

To supply a stable form of glutamine during times of depletion caused by rapid growth, tissue repair or other high metabolic demands to help maintain health (immune support) including the integrity of the intestinal tract and enhance recovery. Supplementation may be especially important when prolonged energy restriction (dieting) is combined with demanding physical stresses.

#### **Potential Beneficiaries**

- Athletes and exercisers under prolonged demanding physical stress, and especially combined with extended periods of energy restriction as in weight/body fat conscious athletes attempting to "make weight" or attain extremely low body fat
- Anyone attempting to support the immune system, intestinal integrity and/or recovery related to
  exercise/physical induced stresses including to reduce the likelihood of overtraining/reaching or attenuate its
  general effects

#### **Unique Features**

- Produced in an easy-to-mix powder that can be added to other desired nutrition products, including sports drinks and shakes
- Effective and safely synergistic with all other dotFIT products
- Contains L-glutamine in a dipeptide patented, stabilized compound (Magnesium-Glycyl-Glutamine) from Albion<sup>60</sup> for potentially greater absorption and ability to reach desired target tissues<sup>67</sup>
- NSF Certified for Sport (NSFCS), which is an additional product guarantee for drug tested athletes. Click <u>here</u> for the dotFIT NSFCS section



• Formulated and manufactured for taste and pleasing texture in a regularly inspected NSF certified facility, in compliance with Good Manufacturing Practices (GMPs) exclusively for dotFIT, LLC

# **Supplement Facts Panel**





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