Patient’s Introduction to Inflammation Therapy

An abridged version of the Physician’s Guide to Inflammation Therapy

[For details of preliminary tests, see Physician’s Guide page 1]

PREPARING FOR I.T.

Light
To avoid photosensitivity symptoms and minimize symptoms caused by an increase in 1,25-D production, reduce exposure to sunlight and bright lights by staying indoors as much as possible and covering up well whenever venturing outside during daylight hours.

Patients who were not photosensitive before treatment may become photosensitive when therapy is initiated. If symptoms exacerbate to intolerable levels, sun or bright light exposure may be the cause. Very photosensitive patients will be less symptomatic if they block natural light in their home and workplace.

It is essential for everyone to protect eyes from sunlight and bright lights by wearing amber sunglasses that block blue light, UVA, UVB, and infrared rays. See Sunglasses for details.

Vitamin D
Reduce 25-D to an optimal 8-15ng/ml to help decrease elevations in 1,25-D and thus reduce inflammatory symptoms.

Steroids
Antibiotics will not be effective while corticosteroids (e.g. prednisone, cortef) are suppressing the immune system. Wean from steroids with the help of Benicar before starting Minocycline.

See the document Weaning from Steroid Medications for specific instructions.

Medications
Discontinue the following medications before starting Benicar:

- Immunosuppressants
- Antibiotics not part of Inflammation Therapy
- Antibacterials: Sulfasalazine, Plaquenil and Methotrexate

Important recommendations regarding other medications:
See Physician’s Guide page 2 for details.

BEGINNING THE TREATMENT

WARNING: Benicar is contraindicated during pregnancy and/or lactation.

Take Benicar 20mg every six hours (q6h), on the first day and every day thereafter.

Benicar/Olmetec/Votum/Olmecip (Olmesartan medoxomil) is the only angiotensin receptor blocker (ARB) recommended. A Benicar/thiazide combination should not be used.

Most patients can tolerate a starting dose of 20mg every six hours but it's okay to start lower and ramp up. Symptoms of dizziness, fatigue or light-headedness are common (with or without low blood pressure) and will usually resolve as therapy continues, but the dose of Benicar may need to be adjusted.
After starting Benicar (or simply reducing vitamin D intake and the level of light), the level of 1,25-D may be rapidly reduced. This often causes temporary neurological-type symptoms such as fatigue, light-headedness, headache, photophobia, etc., as the body adjusts.

Some patients experience an immune system reaction with Benicar alone (or by simply reducing vitamin D intake and the level of light) because Benicar allows the immune system to begin to function normally and kill the pathogenic bacteria. Occasionally these symptoms are intolerable. An increase or decrease in Benicar may be tried to reduce the immune system reaction.

Because frequent, low-dose Minocycline has an anti-inflammatory effect, it may also be used to dampen these symptoms. Taking 25mg of Minocycline q6h or q12h often relieves symptoms that become intolerable.

It usually takes a week or two to stabilize symptoms on Benicar alone. This means that any additional symptoms have waned or resolved, and you feel able to tolerate an increase in symptoms from the expected immune system reactions with pulsed Minocycline.

**Experiment with Benicar dosing**
If you have not yet determined how changing the dose or schedule of Benicar affects symptoms, you should experiment with Benicar before adding Minocycline. Try an extra Benicar, oral and/or sublingual to see if symptoms are reduced. If that isn't effective, increase to every four hours to see if that measure reduces symptoms.

If increasing the Benicar dose doesn't reduce symptoms or seems to increase symptoms, try lowering the dose but continuing a frequency of no less than every eight hours.

**Benicar is continued throughout Inflammation Therapy.**

**ADDING MINOCYCLINE**

**Begin Minocycline at 25mg every other day (qod).**
You should add Minocycline after 1-2 weeks on Benicar alone. It’s okay to start with less than 25mg of Minocycline. Either generic or brand name can be used. Minocycline is only available in 50, 75 and 100mg capsules or tablets. Capsules may be opened to divide the contents into smaller portions to provide the needed dose. Use a pill splitter to cut tablets, or use compounded capsules.

If you were on Benicar while weaning from steroids, continue Benicar for two weeks after weaning, before adding Minocycline.

**Increase Minocycline in 25mg increments from 25mg to 50mg to 75mg to 100mg.**
It’s okay to try a smaller increase.

Allow a week or more between increased doses to make sure the immune system reaction is not more than you wish to tolerate.

Different bacteria and tissues can be targeted by different levels of Minocycline, so there is good reason to stay at each dosing level until the immune system reaction is minimal.

Don’t try to ‘speed up’ therapy by using a higher dose of Minocycline than the minimum needed to elicit a tolerable immune system reaction. These are very slow-growing bacteria, and there is no need to hurry. The dose of Minocycline that can be tolerated may change (both up and down) during the course of therapy.
Ramping too quickly is not advised but there is no need to tarry. You’ll gain confidence in your knowledge of the actions of your immune response and when to increase, as you get more experience in independently adjusting Benicar and Minocycline.

**100mg is the maximum dose of Minocycline.** When this every-other-day dose no longer produces a significant immune system reaction, you’re ready to add a second antibiotic. The details are in the section of this document titled *Adding the Second and Third Antibiotics.*

**Experiment with Minocycline**
For some patients some of the therapy antibiotics may be herx-inducing (increases symptoms) or palliative (reduces symptoms). Before considering the addition of a second antibiotic, you should experiment with Minocycline to see how it works for you.

**When you reach 100mg of Minocycline**, if you have not yet discovered if Minocycline is herx-INducing or herx-REducing for you, you should reduce the Minocycline dose to 25mg for four doses, to see if that dampens or increases symptoms. This will help determine the best strategy to use when adding the second antibiotic. It will also help you decide how to adjust Minocycline when taking two or three antibiotics if symptoms flare to intolerable.

You can also extend the 100mg Minocycline dosing schedule to every three days to see if symptoms are dampened or if more herxing is provoked.

A lower dose of Minocycline every six or 12 hours (25mg q6h or 50mg q12h or a daily dose of 25-50mg) may be trialed to see if this dosing has a palliative effect on symptoms.

Usually, patients who react strongest on the day they take Minocycline find they are in the Mino 'herx-inducer' group, and those whose symptoms increase on the second day find that they are in the 'herx-palliative' group.

**IMMUNE SYSTEM REACTIONS**

Be alert for the temporary worsening of disease symptoms, an immune system reaction called the Jarisch-Herxheimer Reaction ('herx').

Minocycline usually elicits the maximum herx as its tissue concentration decays away to zero. Herxing typically begin 1–24 hours after the Minocycline dose and often lessens 12-24 hours before the next antibiotic dose. Many patients find the reaction is strongest on the second day.

Immune system reaction (herx, immunopathology) is unavoidable and will make you feel worse before you feel better. You need a continued determination to recover your health, and to be prepared to weather the worsening or reappearance of symptoms with optimism, knowing that this will lessen over time, relative to the severity at onset.

An immune system reaction may be an increase in current inflammatory symptoms, a return of previous symptoms or the emergence of new symptoms. Usually these symptoms are merely unpleasant, but they can be temporarily debilitating or serious.

*The goal is to maintain tolerable symptoms at all times.*
If you have **severe cardiac symptoms** you may require immediate intervention. See *Anticipating, Identifying and Treating Cardiac Symptoms.*

If you’ve had a cardiac workup you have the advantage of knowing of the possibility of heart disease and can be prepared with a full spectrum of management techniques and/or guided emergency instructions.

If you’ve had cardio-respiratory, liver or renal involvement or other serious health problems, you should be monitored very closely by your physician during IT.

Immune system reactions can occur at any time and with each increase in a dose. Other factors can also influence herxing, e.g., an increase in body temperature, exposure to light, stress, or remodeled tissues revealing new bacteria.

**If symptoms become intolerable or include significant cardiac or respiratory symptoms:**

- increase Benicar to 20-40mg every four hours around the clock until symptoms subside *if this action has been proven to reduce symptoms*
- reduce light exposure to reduce symptoms
- rest
- take palliative medication (recognizing also that anxiety may exacerbate symptoms)

**Seek emergency medical attention if you have any doubts about the severity of symptoms.**

During a 'crisis' situation, an extra 20mg of Benicar may be chewed and taken sublingually with each every three- or four- hour oral Benicar dose *if this action has proven to reduce symptoms*. This is especially important if you have GI tract inflammation.

If increasing Benicar does not reduce intolerable symptoms enough, **adjust Minocycline with one of the following options**. *Try only one of these options at a time and assess effect before trying another option:*

- do not take the next dose
- reduce the next dose (lowest dose is 25mg)
- extend the schedule to every third or fourth day
- take an extra dose of 25mg (or 50mg if used to a higher dose)
- discontinue Minocycline until symptoms settle
- ramp up the dose by 25mg
- take a lower dose more often (e.g. 25mg every 6 hours or 50mg every 12 hours or a daily dose of 25 or 50mg)

**When uncertain what to do** when trying to reduce symptoms, and increasing Benicar was not sufficient, it’s best to first try reducing the Minocycline dose and/or delaying the next dose before trying an extra dose or frequent Minocycline dosing.

---

© Copyright 2011 Chronic Illness Recovery. All rights reserved.
When symptoms are tolerable, reduce Benicar to every 6 hours. If Minocycline was taken more frequently, gradually lengthen the Minocycline dosing interval back to the optimal 48 hour mark to try to provoke a tolerable immune system reaction.

**Don’t resume ramping Minocycline until symptoms are tolerable with Benicar at your optimum dose/schedule.**

**How to reduce Benicar**

If you’re taking Benicar 40mg every six hours and continue to have difficulty maintaining tolerable symptoms, you should wean the dose to see if less VDR activation reduces symptoms. This is best done with a very slow shift. Reduce the Benicar dose every 6 hours by cutting a little off each of the 40mg tablets to try and get a 35mg dose to take for a week. The crumbs may be saved for sublingual use as needed, but the goal is to reduce how much Benicar is needed in a 24 hour period. When symptoms are tolerable with a 35mg dose, reduce by another 5-10mg for another week. Alternatively, take 20mg every four hours and gradually increase the time between doses until 20mg every six hours is reached.

It's necessary to reduce Benicar very gradually because symptoms may increase temporarily as the anti-inflammatory effect is reduced. You may need to persist through an uncomfortable period of increased symptoms before achieving the desired reduction in symptoms or improvement in lab work.

Supplements such as alpha lipoic acid (ALA), DIM (Diindolylmethane), bromelain, NAC (N-acetylcysteine), milk thistle, chlorogenic acid, or hawthorn can reduce herxing, by blocking NF-kappa B activation (as the higher dose of Benicar does) and are less likely to activate the VDR. Details of these supplements and other possible options (e.g., quercetin, guaifenesin, ginger, garlic, caffeine, bromelain, curcumin, resveratrol, pterostibene. genestein) for temporary symptom palliation are discussed in the complementary document *Herxheimer Symptom Management*.

**ADDING THE SECOND AND THIRD ANTIBIOTICS**

**ASSESSMENT**

**Blood Tests**

Before adding a second antibiotic, your doctor will want to re-assess (or assess) the recommended baseline blood tests. It isn’t necessary to assess the level of 1,25-D at this point because it fluctuates rapidly during treatment. If cost is a factor and if previous tests have been normal, the only essential test is the level of 25-D (if it was elevated or you haven’t been able to avoid light as much as recommended).

**Determining Readiness to Add the Second Antibiotic**

If you’ve been getting tolerable symptoms for a week or two on 100mg Minocycline every other day, it’s time for the addition of a second antibiotic.

Continue Benicar throughout the treatment, light restrictions as needed, and vitamin D avoidance to achieve or maintain 25-D at 8-15ng/ml.

**CHOOSING THE SECOND ANTIBIOTIC**

**Zithromax vs. Clindamycin**

The preferred second antibiotic is Zithromax (generic azithromycin is fine) unless there are special circumstances. Your doctor will evaluate you for cardiac, respiratory and neurological symptoms both before treatment and in response to immune system reactions. See *Physician’s Guide* page 9 for further details.
How to add Clindamycin as a second and third antibiotic is described later in this document.

**ADDING ZITHROMAX**

In the two-antibiotic combination:

- Benicar is continued at your optimal dose and schedule
- Minocycline is taken every other day
- Zithromax is taken every 10 days

Zithromax (azithromycin) greatly potentiates the action of Minocycline and must be added cautiously.

**Basic ramping instructions:** Less than 31.25mg of Zith may be taken initially, if there is a need to be extra cautious. Tablets may be cut with a pill splitter or crushed and divided. 250 mg tablets will be easiest to divide for the initial low doses.

<table>
<thead>
<tr>
<th>Zithromax is increased in 31.25mg increments:</th>
</tr>
</thead>
<tbody>
<tr>
<td>31.25mg = $\frac{1}{8}$ 250mg tablet</td>
</tr>
<tr>
<td>62.50mg = $\frac{1}{4}$ 250mg tablet</td>
</tr>
<tr>
<td>93.75mg = $\frac{3}{8}$ 250mg tablet</td>
</tr>
<tr>
<td>125 mg = $\frac{1}{2}$ 250mg tablet (maximum dose)</td>
</tr>
</tbody>
</table>

You should also adjust the starting dose of Zithromax to the level which is likely to produce the least herxing. Most patients can tolerate the usual starting dose of 31.25mg but others may need a much smaller dose.

If you've had significant cardiac or respiratory symptoms you should start with a tiny dose of Zithromax. Start with 10mg and increase by 10mg increments every 10 days (longer if symptoms aren't tolerable) up to 30mg (then increase by 20mg if symptoms allow). Zithromax comes in powder form which can be mixed into a liquid preparation to facilitate very small doses.

**Adjust the Minocycline Dose**

When adding or increasing Zithromax:

If you’ve assessed that Minocycline is 'herx-inducing' (increases symptoms) for you, you should reduce the dose of Minocycline to 25mg.

If you’ve assessed that Minocycline is 'palliative' (reduces symptoms) for you, you should consider keeping it at 75-100mg.

Note: If you started Zithromax with a higher dose of Minocycline, you should decrease Minocycline to 25mg before increasing Zithromax, because a lower dose of Minocycline is likely to be better at weakening bacteria and it’s important to use all the Minocycline dose levels with each dose of Zithromax to see what herxing can be induced at each dose level. After the first cycle, if symptoms are tolerable begin ramping Minocycline down by 25mg increments. Avoid reducing Mino on the days Zith usually peaks (often on days 3-6 and 9). Then, follow the usual ramping schedule as described below.

**Do not ramp Minocycline until the second cycle.**

**Do not increase Zithromax until symptoms have been tolerable with 100mg Minocycline every other day for an entire 10-day cycle.**

*Always base Zithromax ramping readiness on tolerable symptoms.* If you are able to tolerate a slow and steady ramping schedule without the need to slow down the immune system response, you will reach maximum doses of Minocycline and Zithromax in *not less than 3 months.*
Many patients will need to proceed more slowly, so the dose of Minocycline may not change on schedule, or may go down and then back up to keep symptoms tolerable. Also, Zithromax dosage may not change on day one of many 10-day cycles.

You should use past experience to avoid ramping Minocycline on the days Zithromax peaks (usually, but not always, days 3-6 and day 9).

When taking Zithromax you will have to live with and manage the immune system response consequences for some days or even weeks. Reactions to Minocycline plus Zithromax may vary with each cycle. It’s typical of Zithromax to provoke the most powerful immune system response as its serum concentration is waning, but reactions can occur at any time during the dosing cycles and with each increase in dosage.

With the addition of Zithromax, it is not unusual to develop new, sometimes alarming, symptoms because this antibiotic combination eliminates organisms that were not susceptible to Minocycline alone.

It is important to manage the antibiotics doses using incremental dosing levels which control the immune response and avoid uncomfortable reactions. It is fine to ramp slowly. If immune system reactions are occurring, intracellular bacteria are being eliminated. There is no advantage to increasing the antibiotics too quickly.

To prevent medication error, use a pillbox reminder and keep a record of Minocycline and Zithromax doses.

**Carefully follow the instructions for introducing and increasing Zithromax to avert any serious problems.**

**PATIENT GUIDE TO MAXIMUM RAMPING SPEED OF ZITHROMAX FOR THOSE ABLE TO USE A STARTING DOSE OF 25MG MINOCYCLINE AND 31.25MG ZITHROMAX**


### HOW TO MANAGE THE ZITHROMAX IMMUNE SYSTEM RESPONSE

**If symptoms become intolerable, follow the previous instructions on managing the immune response.** If adjusting the dose of Benicar, rest, reduced light exposure, palliative medications, and adjusting Minocycline do not reduce intolerable symptoms, **adjust the dose and/or schedule of Zithromax.**

**To reduce symptoms, adjust Zithromax with the following options:**
- decrease the next dose
- take an early dose (the same or reduced) if symptoms peak on days 8-10
- delay the next dose

Note: Delaying the Zithromax dose can increase symptoms because Zithromax may be even more effective as the tissue concentration wanes. **In that case, taking a lower dose of Zithromax, if intolerable symptoms persist, may work better.**

**If Benicar was increased, don’t increase Minocycline or Zithromax until symptoms are, once more, tolerable with Benicar 40mg q6h or your optimal Benicar dose/schedule.**

**How to Discontinue Zithromax**

When symptoms are impossible to control with the addition of Zithromax, it may be discontinued. This will often result in a temporary worsening of symptoms, particularly from days 10-12 (possibly as long as four weeks), as the concentration of Zithromax slowly dissipates from the tissues. During this time, follow the recommendations to manage the immune response and palliate symptoms as needed.
**ADDING CLINDAMYCIN AS THE SECOND ANTIBIOTIC (INSTEAD OF ZITHROMAX)**

In this two-antibiotic combination:
- Benicar is continued at your optimal dose/schedule
- Clindamycin is taken at the same time as Minocycline every other day

Generic Clindamycin or brand name (Cleocin, Dalacin) are acceptable. 150mg capsules will be easier to divide initially.

Clindamycin is increased by 37.5mg increments:
- 37.5mg (1/4 capsule)
- 75mg (1/2 capsule)
- 112.5mg (3/4 capsule)
- 150mg (full capsule) This is the maximum dose.

Clindamycin may be started at, and increased in, smaller increments or very tiny doses.

When adding Clindamycin: if you've assessed that Minocycline is 'herx-inducing' (increases symptoms) for you, you should reduce the dose of Minocycline.

If you’ve assessed that Minocycline is 'palliative' (reduces symptoms) for you, you should consider keeping it at 100mg. Note: If you started Clindamycin with a higher dose of Minocycline, you should decrease Minocycline to 25mg at some point because a lower dose of Minocycline is likely to be better at weakening bacteria and it's important to use all the Minocycline dose levels with each dose of Clindamycin to see what herxing can be induced at each dose level.

Minocycline is ramped in 25mg increments to a maximum dose of 100mg.

There is no one preferred or recommended ramping method. Minocycline and Clindamycin may be increased in any order but they should be ramped **one at a time**. After you’ve made an adjustment and assessed the response, you may find you prefer one pattern of ramping. Only the dose level is varied, not the every-other-day schedule.

Stay at each dosage for a minimum of 3 - 4 doses with tolerable symptoms **at all times** before increasing, unless experience indicates that an increase would dampen intolerable symptoms.

Clindamycin may provoke an immune response immediately or it may take a few weeks to provoke a reaction. Be alert for an increase in psychological symptoms such as depression, insomnia, anxiety, moodiness, obsessive-compulsive behavior, irritability and anger.

*If symptoms become intolerable, follow the previous instructions on managing the immune response.* If adjusting the dose of Benicar, rest, reduced light exposure, palliative medications, and adjusting Minocycline do not reduce intolerable symptoms, **adjust the dose or schedule of Clindamycin see Physician’s Guide page 14.**

Previous instructions regarding adjusting Minocycline may also be followed to reduce immune system reaction symptoms.

**Don’t increase Minocycline or Clindamycin until symptoms are tolerable again with Benicar at your optimal dose/schedule.**

**HOW TO TRANSITION FROM MINOCYCLINE AND CLINDAMYCIN TO MINOCYCLINE AND ZITHROMAX**

See **Physician’s Guide** page 15.
ADDING THE THIRD ANTIBIOTIC

In this three-antibiotic combination:
- Benicar is continued at your optimal dose/schedule
- Minocycline is taken every other day
- Zithromax is taken every 10 days
- Clindamycin is taken every other day

When the maximum doses of Minocycline and Zithromax no longer provoke significant herx, it’s time to add Clindamycin.

When adding Clindamycin as the third antibiotic:
If you’ve assessed that Minocycline is ‘herx-inducing’ (increases symptoms) for you, you should reduce the dose of Minocycline. But if you’ve assessed that Minocycline is ‘palliative’ (reduces symptoms) for you, you should consider keeping it at 100mg. Also, the dose of Zithromax should be adjusted to the level which is likely to produce the least herxing. If you start with a higher dose of Zithromax, you’ll need to ramp it slowly downward (and then back up) because different bacteria succumb to different levels of Zithromax.

Clindamycin and Minocycline are taken together on day one of the 10-day Zithromax cycle and then every other day.

Ramp up Minocycline by 25mg increments, to a maximum dose of 100mg every other day.

Ramp up Zithromax by 31.25mg (or smaller) increments every 10 days, to a maximum dose of 125mg.

The starting dose of Clindamycin is 37.5mg (1/4 or 1/8 or less of a 150mg capsule).

Ramp up Clindamycin by 37.5mg increments (or smaller), to a maximum dose of 150mg every other day.

Clindamycin may be started, and increased, in smaller increments or very tiny doses.

Ramp only one antibiotic (Minocycline, Zithromax, Clindamycin) at a time. Proceed cautiously with the ramping schedule because this new combination may take a few days to provoke an immune response.

Minocycline and Clindamycin can be adjusted more quickly than Zithromax, and often have a modulatory effect on the immune response, so it’s easier to control symptoms by adjusting Minocycline and Clindamycin.

For ramping options, see Physician’s Guide page 16.

The maximum end doses of this three-antibiotic combination are:
- 125 mg of Zithromax
- 150mg of Clindamycin
- 100mg Minocycline

Continue this optimal target combination of 100mg Minocycline every other day, plus 150mg Clindamycin every other day, plus 125mg Zithromax every 10 days, for as long as it provokes an immune system response. This may be many months. If there is no Herx reaction, continue for up to 3 months to assess the response.

The Minocycline and/or Clindamycin schedule may also be extended to every 3 days in an effort to provoke stronger immune response.

125mg is the maximum dose of Zithromax when taking three antibiotics.
OTHER THREE-ANTIBIOTIC COMBINATIONS

Because there are many species of intracellular bacteria that cause inflammatory illnesses, a variety of antibiotic combinations is needed to eliminate all of them. When the Minocycline, Zithromax and Clindamycin combination no longer provokes an immune response, other antibiotic combinations should be used.

All antibiotic combinations should include every-other-day Minocycline or Demeclocycline because these tetracyclines are the primary, synergistic antibiotics.

Adjust all antibiotics to doses that have been assessed to cause the least herxing when a new combination is begun, and then ramp up one antibiotic at a time as symptoms allow.

It is important to choose doses and combinations - at any point in time - which result in symptoms that are tolerated. Eventually all the antibiotic combinations detailed in the Physician's Guide should be used, until none provokes an immune response. It may take several years to complete the treatment, but significant symptom resolution is usually accomplished much earlier.

For details see Physician’s Guide page 17.

TREATMENT END MARKERS

- resolution of systemic symptoms
- return of physical function
- absence of an immune system reaction to treatment medications
- return of baseline lab markers to normal
- signs of inflammation resolution on CT and MRI imaging

Disclaimer: This treatment guide may be used by medical practitioners and patients. It is essential for safety and efficacy that patients clearly understand all aspects of this treatment and how to get professional help should they need it. This document contains statements pertaining to the expected results of Inflammation Therapy. These statements are guided by past experience and/or based on pertinent anecdotal evidence. The words or phrases ‘ought to’, ‘should’, ‘could’, ‘may’, or similar expressions are intended to identify those statements. Individual patient results may differ.

This document contains statements which represent scientific theories supported by the medical literature and molecular modeling by an independent researcher, that are not yet generally accepted by the scientific community. These theories and research fit the medical model of Inflammation Therapy which has provided considerable supporting anecdotal evidence. We make no claims as to the accuracy of these statements and they will be updated whenever new information becomes available.

Chronic Illness Recovery Inc. does not engage in the practice of medicine. This document is for educational purposes only. All ingestion of pharmaceutical drugs mentioned in this document must be made under the supervision of a registered medical practitioner.