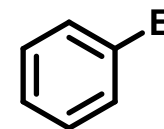
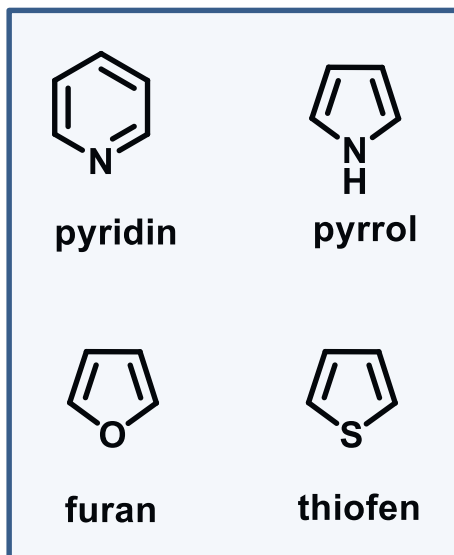
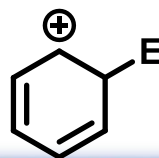


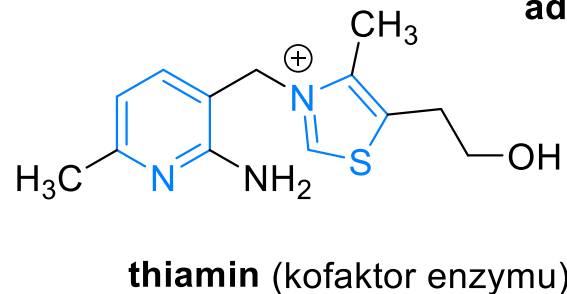
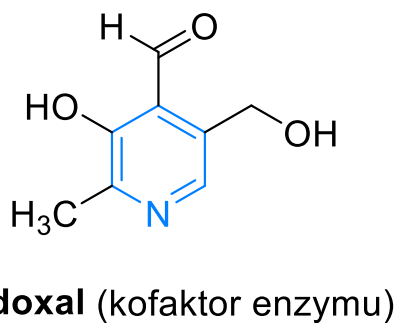
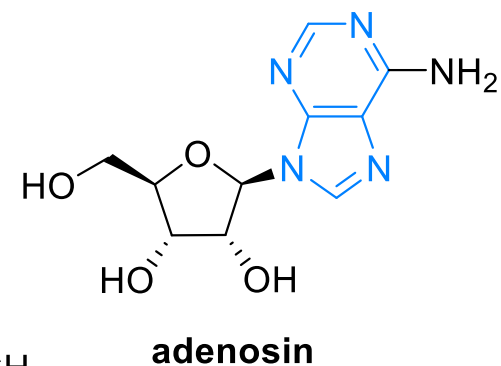
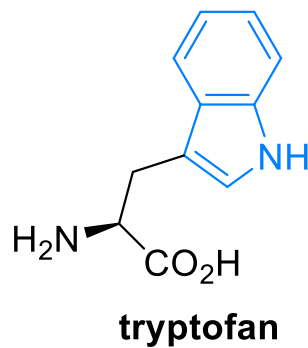
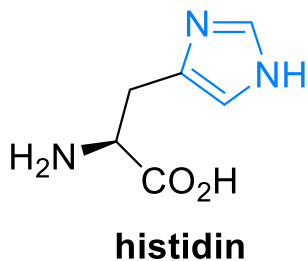


# 7. Areny

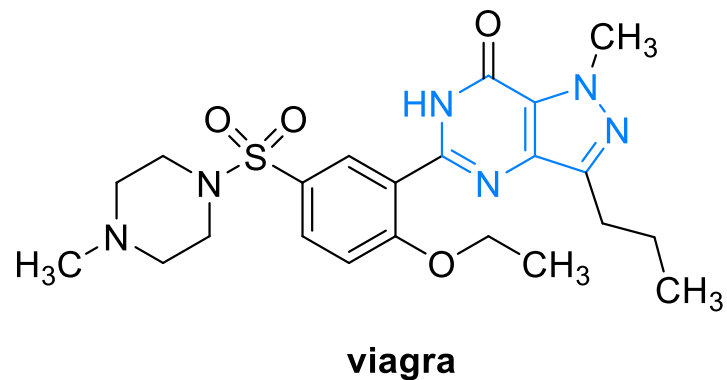
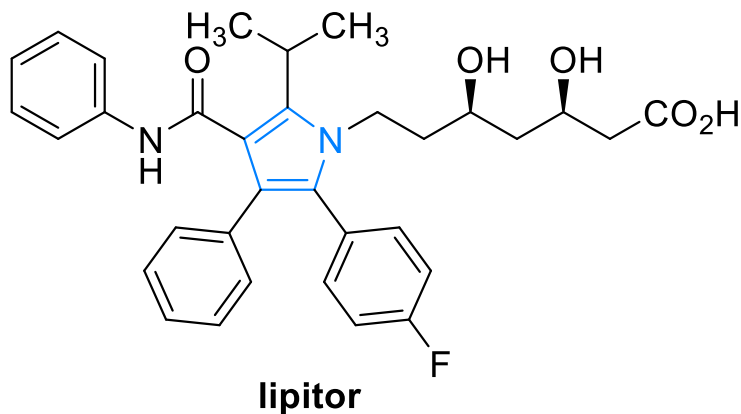




- důležité strukturní a funkční elementy biomolekul (enzymy, DNA, RNA ...)

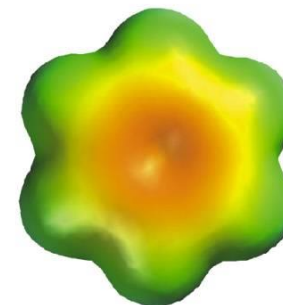
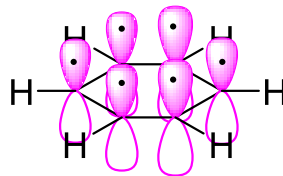
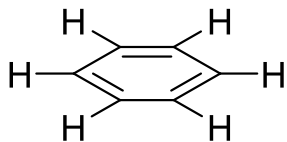
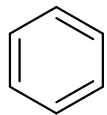


- běžná součást léčiv

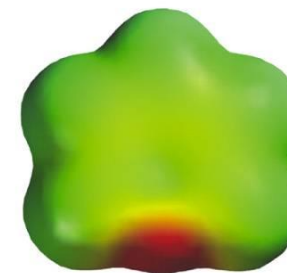
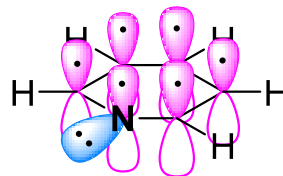
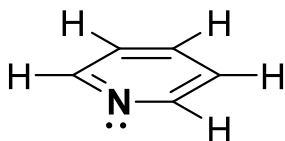
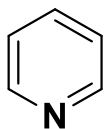




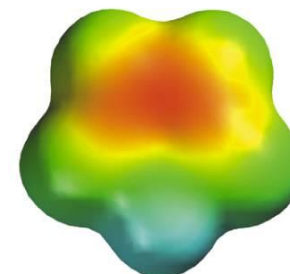
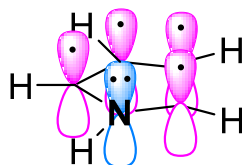
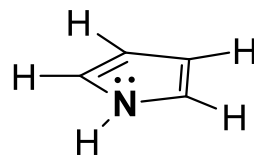
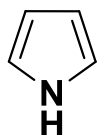
- Srovnání struktury benzenu, pyridinu, a pyrrolu



benzene



pyridine



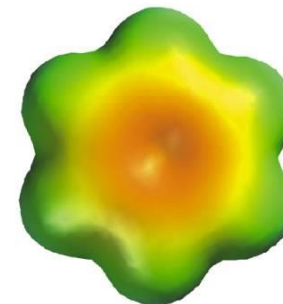
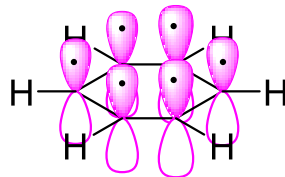
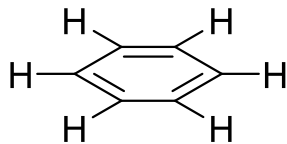
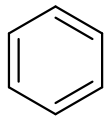
pyrrole

Q: jaký vliv budou mít tyto rozdíly na reaktivitu?

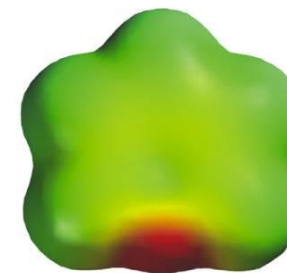
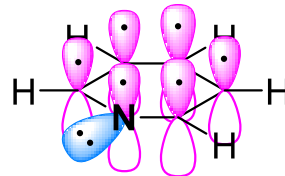
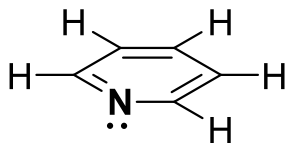
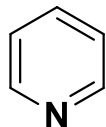
 $\delta^-$  $\delta^+$



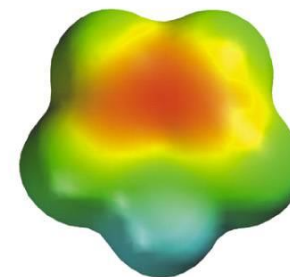
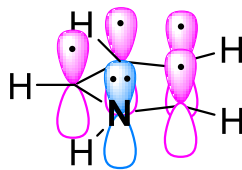
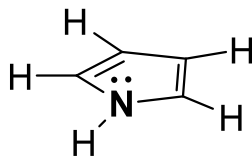
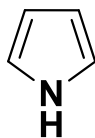
- Srovnání struktury benzenu, pyridinu, a pyrrolu



benzene



pyridine



pyrrole

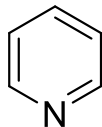
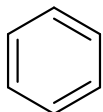
Q: jaký vliv budou mít tyto rozdíly na reaktivitu?





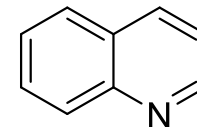
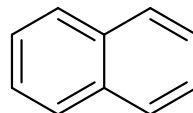
- přítomnost heterocyklického motivu často významně ovlivňuje:

### rozpustnost ve vodě



benzen  
1,79 g/l H<sub>2</sub>O

pyridin  
rozpustný v H<sub>2</sub>O

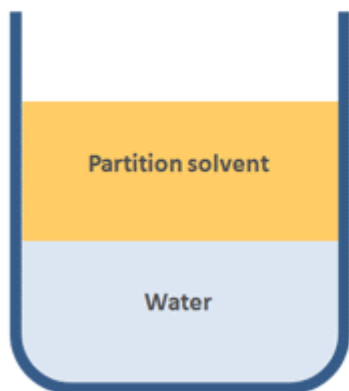


naftalen  
0,03 g/l H<sub>2</sub>O

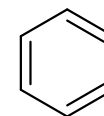
chinolin  
6,65 g/l H<sub>2</sub>O

**hydrofilní vs lipofilní vlastnosti:** velmi důležitý parametr při optimalizaci léčiv

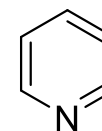
$P = \text{Partition Coefficient} = \frac{\text{Concentration dissolved in partition solvent}}{\text{Concentration dissolved in water}}$



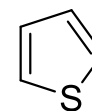
Conditions:  
The solvents are "immiscible"  
The system must be at equilibrium  
All the solute must be dissolved  
Temperature should be constant



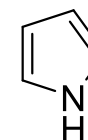
log P = 2.12



log P = 0.65



log P = 1.79

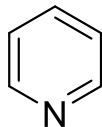
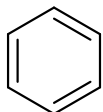


log P = 0.75



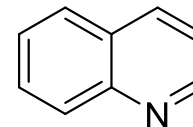
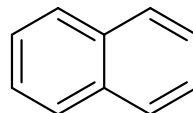
- přítomnost heterocyklického motivu často významně ovlivňuje:

### rozpustnost ve vodě



benzen  
1,79 g/l H<sub>2</sub>O

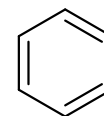
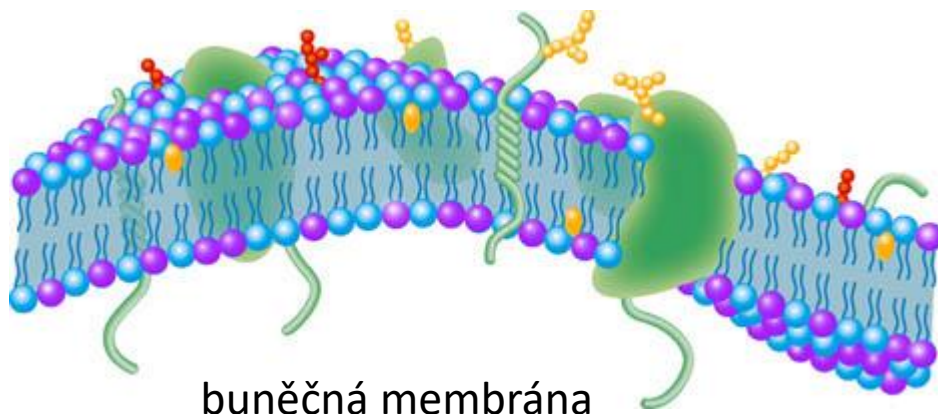
pyridin  
rozpustný v H<sub>2</sub>O



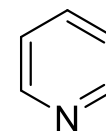
naftalen  
0,03 g/l H<sub>2</sub>O

chinolin  
6,65 g/l H<sub>2</sub>O

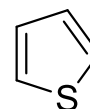
**hydrofilní vs lipofilní vlastnosti:** velmi důležitý parametr při optimalizaci léčiv



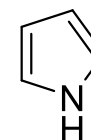
log P = 2.12



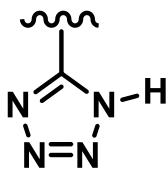
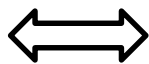
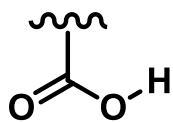
log P = 0.65



log P = 1.79



log P = 0.75

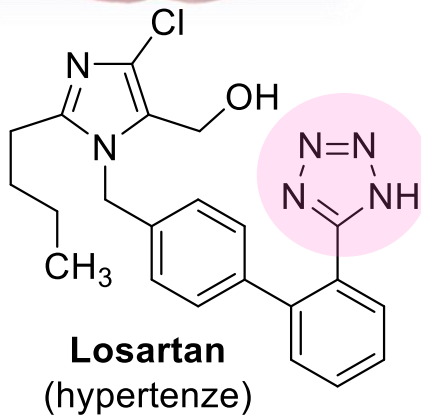
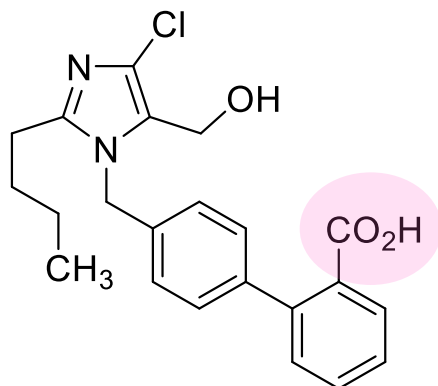
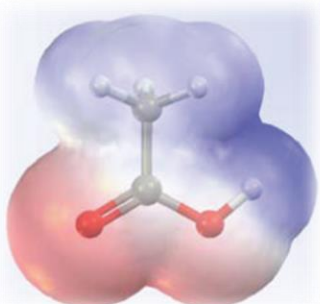


karboxylová  
skupina

pKa = 4.5

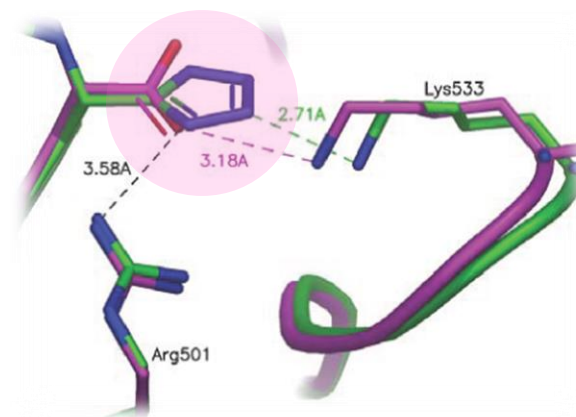
tetrazol

pKa = 4.75

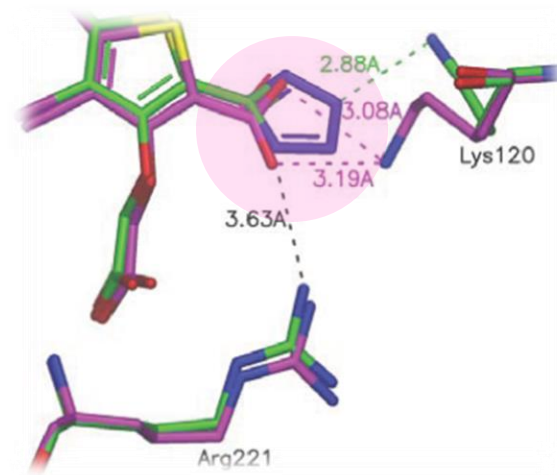


## Analogická interakce s proteiny

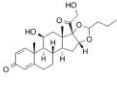
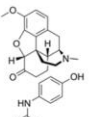
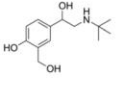
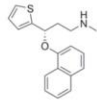
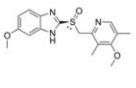
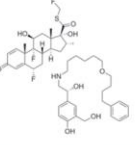
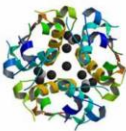
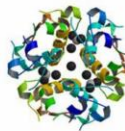
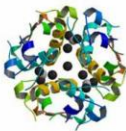
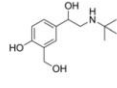
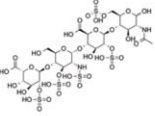
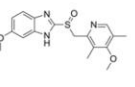
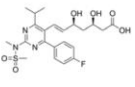

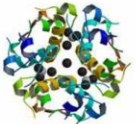
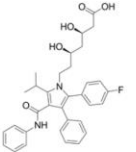
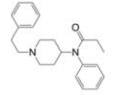
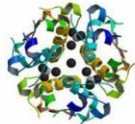
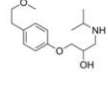
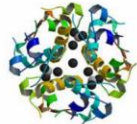
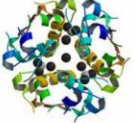
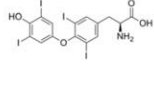
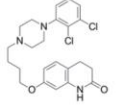
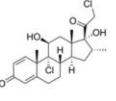
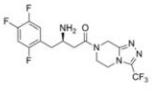
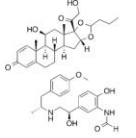
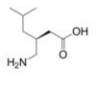
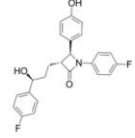

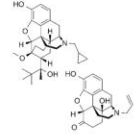
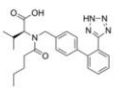
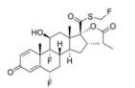
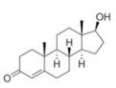
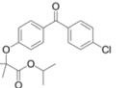


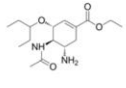
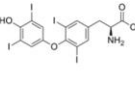
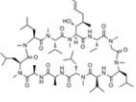

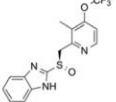
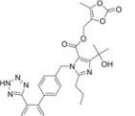
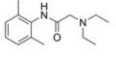
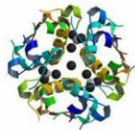
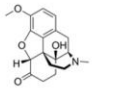
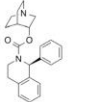
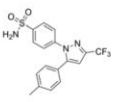
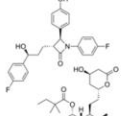
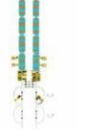
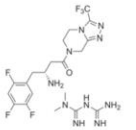
Ilustrace 1



Ilustrace 2





<p><b>1 Budesonide</b> (Budesonide)</p>  <p>ALM DER RES Approved 1997</p>	<p><b>2 Hydrocodone/APAP</b> (Hydrocodone &amp; Acetaminophen)</p>  <p>Nervous System Approved 1982</p>	<p><b>3 Proair HFA</b> (Salbutamol)</p>  <p>Respiratory System Approved 2004</p>	<p><b>4 Cymbalta</b> (Duloxetine)</p>  <p>Nervous System Approved 2004</p>	<p><b>5 Nexium</b> (Esomeprazole)</p>  <p>Alimentary Tract &amp; Metabolism Approved 2001</p>	<p><b>6 Advair Diskus</b> (Fluticasone Propionate &amp; Salmeterol)</p>  <p>Respiratory System Approved 2000</p>	<p><b>7 Lantus</b> (Insulin Glargine)</p>  <p>Endocrine System Approved 2000</p>	<p><b>8 Lantus SoloSTAR</b> (Insulin Glargine)</p>  <p>Endocrine System Approved 2000</p>	<p><b>9 OneTouch</b> (Insulin Glargine)</p>  <p>Endocrine System Approved 2006</p>	<p><b>10 Ventolin HFA</b> (Salbutamol)</p>  <p>Respiratory System Approved 2001</p>
<p><b>11 Enoxaparin</b> (Enoxaparin)</p>  <p>BBO MSK Approved 1993</p>	<p><b>12 Omeprazole</b> (Omeprazole)</p>  <p>Alimentary Tract &amp; Metabolism Approved 1989</p>	<p><b>13 Crestor</b> (Rosuvastatin)</p>  <p>BBO CAR Approved 2003</p>	<p><b>14 Spiriva</b> (Tiotropium)</p>  <p>Respiratory System Approved 2004</p>	<p><b>15 Levemir</b> (Insulin Detemir)</p>  <p>Endocrine System Approved 2005</p>	<p><b>16 Atorvastatin</b> (Atorvastatin)</p>  <p>BBO CAR Approved 1996</p>	<p><b>17 Fentanyl</b> (Fentanyl)</p>  <p>NER ONC Approved 1968</p>	<p><b>18 NovoLog FlexPen</b> (Insulin Aspart)</p>  <p>Endocrine System Approved 2000</p>	<p><b>19 Metoprolol</b> (Metoprolol)</p>  <p>Cardiovascular System Approved 1978</p>	<p><b>20 NovoLog</b> (Insulin Aspart)</p>  <p>Endocrine System Approved 2000</p>
<p><b>21 Humalog</b> (Insulin Lispro)</p>  <p>Endocrine System Approved 1996</p>	<p><b>22 Synthroid</b> (Levothyroxine)</p>  <p>Endocrine System Approved 2002</p>	<p><b>23 Abilify</b> (Aripiprazole)</p>  <p>Nervous System Approved 2002</p>	<p><b>24 Nasonex</b> (Mometasone)</p>  <p>Respiratory System Approved 1997</p>	<p><b>25 Januvia</b> (Sitagliptin)</p>  <p>Endocrine System Approved 2006</p>	<p><b>26 Symbicort</b> (Budesonide &amp; Formoterol)</p>  <p>Respiratory System Approved 2006</p>	<p><b>27 Lyrica</b> (Pregabalin)</p>  <p>MSK NER Approved 2004</p>	<p><b>28 Zeltia</b> (Ezetimibe)</p>  <p>BBO CAR Approved 2002</p>	<p><b>29 Namenda</b> (Memantine)</p>  <p>Nervous System Approved 2003</p>	<p><b>30 Suboxone</b> (Buprenorphine &amp; Naloxone)</p>  <p>Nervous System Approved 2002</p>
<p><b>31 Diovan</b> (Valsartan)</p>  <p>CAR END Approved 1996</p>	<p><b>32 Flovent HFA</b> (Fluticasone Propionate)</p>  <p>Respiratory System Approved 1996</p>	<p><b>33 AndroGel</b> (Testosterone)</p>  <p>Genito-Urinary &amp; Sex Hormone Approved 2000</p>	<p><b>34 Fenofibrate</b> (Fenofibrate)</p>  <p>BBO CAR END Approved 1993</p>	<p><b>35 Remicade</b> (Infliximab)</p>  <p>END MSK Approved 1998</p>	<p><b>36 OneTouch Ultra</b></p>  <p>Endocrine System Marketed 2006*</p>	<p><b>37 Tamiflu</b> (Oseltamivir)</p>  <p>Anti-Infective Approved 1999</p>	<p><b>38 Levothyroxine</b> (Levothyroxine)</p>  <p>Endocrine System Approved 2000</p>	<p><b>39 Restasis</b> (Cyclosporine)</p>  <p>Sensory Organ Approved 2002</p>	<p><b>40 Lovaza</b> (Omega 3-Acid Ethyl Esters)</p>  <p>Cardiovascular System Approved 2004</p>
<p><b>41 Dextilant</b> (Dexlansoprazole)</p>  <p>Alimentary Tract &amp; Metabolism Approved 2007</p>	<p><b>42 Benicar</b> (Olmesartan)</p>  <p>CAR END Approved 2002</p>	<p><b>43 Lidoderm</b> (Lidocaine)</p>  <p>CAR DER NER RES SEN Approved 1948</p>	<p><b>44 Humalog KwikPen</b> (Insulin Lispro)</p>  <p>Endocrine System Approved 1996</p>	<p><b>45 Oxycontin</b> (Oxycodone)</p>  <p>END MSK Approved 2010</p>	<p><b>46 VESicare</b> (Solifenacin)</p>  <p>Genito-Urinary &amp; Sex Hormone Approved 2004</p>	<p><b>47 Celebrex</b> (Celecoxib)</p>  <p>MSK ONC Approved 1998</p>	<p><b>48 Vytorin</b> (Ezetimibe &amp; Simvastatin)</p>  <p>BBO CAR Approved 2004</p>	<p><b>49 Enbrel</b> (Etanercept)</p>  <p>Musculo-Skeletal System Approved 1998</p>	<p><b>50 Janumet</b> (Metformin &amp; Sitagliptin)</p>  <p>Alimentary Tract &amp; Metabolism Approved 2007</p>